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Re-evaluation Note REV2009-02

Preliminary Risk and Value Assessments of Methomyl

(publié aussi en français)

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Foreword

The purpose of this document is to inform registrants, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has completed a preliminary risk assessment of methomyl.

This Re-evaluation Note provides a summary of this preliminary assessment based on data and information reviewed. The preliminary assessments identified potential risks to the general population through dietary and drinking water exposure and to the environment. The PMRA is requesting further data/information to complete the risk and value assessments and propose regulatory action.

The PMRA is soliciting information that may be used to refine this preliminary assessment and/or mitigate risks. The PMRA will accept information up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

The PMRA will review the information received, revise the risk and value assessments as necessary and propose regulatory action in a future document.

1.0 Purpose

This document describes the Pest Management Regulatory Agency preliminary risk and value assessments of the insecticide methomyl and its end-use products. It includes a human health assessment, an environmental assessment and information on the value of methomyl to pest management in Canada. By way of this document, the PMRA is soliciting comments on and input for the risk and value assessments of methomyl from interested parties. Such comments and input could include additional data or information to further refine the risk assessments (e.g. dietary and drinking water), such as typical use pattern information, percent crop treated, area treated per day, number of applications, rates, etc. Comments and input could address the PMRA's risk-assessment approaches and assumptions as applied to methomyl. Further information on the viability of registered alternatives could refine the value assessment.

2.0 Re-evaluation of Methomyl

Methomyl is one of the pesticides subject to re-evaluation in Canada as announced in Re-evaluation Document REV99-01, *Re-evaluation of Organophosphate Pesticides*. Methomyl is a broad spectrum systemic carbamate insecticide belonging to the resistance management Mode of Action (MoA) Group 1A and is an acetylcholinesterase inhibitor. It works by contact and stomach action.

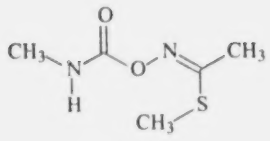
Following the re-evaluation announcement for methomyl, E.I. Du Pont Canada Company, the registrant of the technical grade active ingredient and primary data provider in Canada, indicated it intended to provide continued support for all uses included on the label of commercial class and restricted class end-use products.

2.1 Identity of the Active Substance

Active substance:	Methomyl
Function:	Insecticide
Chemical names:	—
International Union of Pure and Applied Chemistry (IUPAC):	*S*-methyl-*N*-(methylcarbamoyloxy)thioacetimidate
Chemical Abstracts Service (CAS):	methyl *N*-[[(methylamino)carbonyl]oxy]ethanimidothioate
Chemical class:	Carbamate
CAS Number:	16752-77-5
Molecular formula:	$C_5H_{10}N_2O_2S$

Molecular Weight: 162.2 amu

Structural Formula:



Identity of relevant impurities of toxicological, environmental and/or other significance:

Impurities of toxicological concern (as identified in Section 2.13.4 of Regulatory Directive DIR98-04) or Toxic Substances Management Policy (TSMP) Track 1 substances (as identified in Appendix II of DIR99-03) are not expected to be present in the starting materials used to manufacture the product nor are they expected to be formed during the manufacturing process.

2.2 Physiochemical Properties of Active Substance and Interpretation

Property	Result
Vapour pressure at 25°C	0.72 mPa
Henry's law constant	2.13×10^{-6} Pa m^3 mol^{-1}
Ultraviolet (UV)/visible spectrum	Not expected to absorb UV at $\lambda > 350$ nm
Solubility in water at 25°C	57.9 g/L
n-octanol–water partition coefficient (log K_{ow})	log $K_{ow} = 0.093$
Dissociation constant	Not applicable, molecule has no dissociable moiety

2.3 Description of Registered Methomyl Uses

Appendix I lists all methomyl products that are registered under the authority of the *Pest Control Products Act*. Appendix II lists all the uses for which methomyl is presently registered. All uses were supported by the registrant at the time of the initiation of re-evaluation and were, therefore, considered in the health and environmental risk assessments of methomyl. Also presented is whether the use was added through the PMRA Minor Use Program. While supported by the registrant, the data supporting the use was originally generated by a user group.

Uses of methomyl belong to the following use-site categories: Forest and Woodlots, Greenhouse Food Crops, Terrestrial Food Crops and Structural (i.e. farm buildings).

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for methomyl was conducted. With the exception of a comparative cholinesterase study, the database for methomyl is complete and consists of the full array of toxicity studies currently required for hazard-assessment purposes. All of these toxicity studies were conducted in accordance with accepted international testing protocols and good laboratory practices at that time. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to methomyl.

In acute toxicity studies, methomyl technical is highly toxic by the oral route, moderately toxic via the inhalation route and of low toxicity by the dermal route of administration. Acute toxic effects include tremors, salivation, miosis, incoordination, lethargy and breathing difficulties. Methomyl is considered to be non-irritating and non-sensitizing but highly toxic via ocular exposure.

Pharmacokinetic studies in the rat and monkey show that methomyl is rapidly absorbed and predominantly eliminated in the urine and expired air with a minimal amount excreted in the faeces. Methomyl does not appear to accumulate appreciably in tissues. Excretion patterns do not appear to be significantly influenced by species, sex, dose level or duration of dosing. There are three metabolic pathways for methomyl:

- the displacement of the *S*-methyl moiety by glutathione and enzymic transformation to give the mercapturic derivative;
- hydrolysis releasing methomyloxime which is rapidly broken down to carbon dioxide; and
- in vivo isomerization of syn-methomyl to the anti-methomyl isomer which upon hydrolysis produces anti-methomyloxime; this metabolite may then undergo a Beckman rearrangement and elimination reaction to form acetonitrile.

Methomyl, a *S*-methyl carbamate, has consistently demonstrated clinical signs of toxicity indicative of anticholinesterase activity. This effect on cholinesterase activity was noted in various species throughout the database and was typical of the signs identified for the *S*-methyl carbamate class of chemicals. When reviewing the toxicity studies for methomyl, a notable difference was observed between the effects of gavage and dietary dosing. Greater cholinergic toxicity with gavage dosing was attributed to higher peak exposures than those obtained in dietary studies. Clinical signs and cholinesterase inhibition were rarely seen in dietary studies because of the rapid reversibility that likely occurred during periods of feeding. Rats tolerated chronic dietary dose levels that were equivalent to or even exceeded the lethal dose to 50% (LD_{50}) of rats from acute gavage studies. Repeat-dose dietary administration pointed to an effect on erythropoiesis. Anemia and/or pathology of the spleen and bone marrow were noted across species (rat, mouse and dog). Comparison of the dietary short-term and long-term studies in the rat did not suggest a pronounced increase in toxicity with increased duration of dosing. No pronounced gender or species differences were apparent.

Administration of methomyl to hens in an acute delayed neurotoxicity study illustrated no evidence of delayed neurotoxicity. In an acute neurotoxicity study in the rat, cholinesterase inhibition was the most sensitive endpoint with clinical signs of tremors occurring at higher doses. All effects were noted shortly after dosing with animals rapidly returning to normal by 24 hours. In a subchronic neurotoxicity study in the rat, clinical signs were more pronounced than levels of cholinesterase inhibition. No neuropathology findings were noted in the database.

Numerous studies were available on the mutagenic potential of methomyl. Tests included gene mutation, deoxyribonulceic acid (DNA) damage studies, structural chromosome aberrations along with other mutagenic mechanisms. Methomyl did not show mutagenicity or cause primary DNA damage in bacterial or mammalian cells in vitro. It did show mutagenic potential in human lymphocytes in vitro as indicated by an increase in micronuclei and chromosomal aberrations. Positive results were also obtained for DNA damage in vivo in the mouse. Methomyl, however, did not show evidence of carcinogenicity in the mouse or rat.

Methomyl is a metabolite of and is structurally-related to thiodicarb, a pesticide classified as a B2 carcinogen by the Unites States Environmental Protection Agency (USEPA). However, thiodicarb is not a degradate of methomyl, thus tempering this concern. Two animal metabolites of methomyl of potential concern are acetamide and acetonitrile. Acetamide has been classified as a group C possible human carcinogen by the USEPA. The USEPA concluded that acetamide in the diet was not a carcinogenic hazard for the following reasons:

- the conversion rate of methomyl to acetamide is low (~2–3%) and, therefore, residue levels should be low;
- the carcinogenicity studies with methomyl were negative;
- methomyl is comprised of 98.7% syn-isomer and 0.092% anti-isomer, syn-isomer must be converted to anti-isomer before acetamide is formed; and
- acetamide induced liver tumours in rats only when administered at very high dosages, i.e. >1000 mg/kg bw/day.

The USEPA also concluded that acetonitrile in the diet was not a carcinogenic hazard because it is volatile, its residues are small, it has little or no cancer potential and its toxicity was accounted for in the negative methomyl carcinogenicity studies. Lastly, it has been shown in the literature that synthesized nitrosomethomyl is mutagenic in vitro and is capable of producing stomach tumours in rats. However, when methomyl is incubated with nitrite and macerated meat under simulated stomach conditions, there is no evidence that nitrosomethomyl is formed. In summary, methomyl is not considered to pose a carcinogenic risk to humans based on the available data.

No evidence of sensitivity of the young was seen in the multigeneration reproduction study. Effects at the lowest dose tested in the parents and offspring were limited to reduced weight gains. Birth weights were reduced at levels causing maternal toxicity including reduced weight gain and food intake in both generations, and anemia and some clinical signs (body tics) in the first generation. More severe effects were noted at the highest dose in parents (clinical signs) and offspring (increased stillborn and decreased pup survival). Developmental studies in rats and rabbits did not show evidence of sensitivity of the young following in utero exposure. The pronounced difference between gavage and dietary dosing was evident in the rat developmental

studies with an approximate 10-fold higher toxicity with gavage dosing. Malformations were noted in the rat gavage study, but only at levels causing severe maternal toxicity including death. Studies in rabbits did not elicit any teratogenic effects, but clinical signs indicating neurotoxicity were visible at high doses. An increase in variations was seen in the rabbit, but only at a maternally toxic dose. Although sensitivity of the young was not seen in the reproduction and developmental toxicity studies, it should be noted that cholinesterase activity was not assessed in these studies, precluding a definitive assessment of sensitivity.

Reports on accidental and suicidal poisonings in humans with methomyl provide some information on effect levels. Three out of five victims of an accidental poisoning died within three hours of ingestion. It was estimated that individuals ingested between 12–15 mg/kg bw indicating comparable acute toxicity to the rat. Survivors of accidental and attempted suicidal poisonings tended to recover from clinical symptoms (following gastric lavage and atropinization) within 24–48 hours with blood levels of methomyl showing a similar recovery.

Results of the acute and chronic tests conducted on laboratory animals with methomyl technical, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix III and IV.

***Pest Control Products Act* Hazard Characterization**

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of and toxicity to infants and children and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the exposure of and toxicity to infants and children, data of high quality were available for methomyl. The database included one developmental toxicity study in rats, one developmental toxicity study in rabbits and one multigeneration reproduction study in rats.

With respect to potential prenatal and postnatal toxicity, the prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of fetuses to in utero exposure. In the multigeneration reproduction study, severe effects were noted at the highest dose level both in the parents (reduced weight gain, food consumption and clinical signs) and in the offspring (increased stillborn and decreased pup survival). In the rat developmental study, malformations occurred at levels causing severe maternal toxicity including death. While malformations are considered serious, the degree of concern is tempered by the accompanying maternal toxicity. It is recognized that maternal toxicity of such severity could, in and of itself, bring about adverse consequences in the young. Studies in rabbits did not elicit any teratogenic effects, but clinical signs indicating neurotoxicity were visible at high-dose levels. An increase in fetal variations was seen in the rabbit developmental study, but only at a maternally toxic dose. Although sensitivity of the young was not observed in the database, the lack of cholinesterase measurements in this subpopulation precluded a definitive assessment of sensitivity. In the absence of a trigger for this information, it was not deemed necessary to retain the *Pest Control Products Act* factor.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects. However, MOEs less than the target MOE require measures to mitigate (reduce) risk.

3.2.1 Toxicology Endpoint Selection for Occupational Risk Assessment

Short-, Intermediate- and Long-term Dermal Risk Assessment

To assess farmer mixer /loader/applicator (M/L/A), custom M/L/A and postapplication workers

For short-, intermediate- and long-term dermal risk assessment, the results of two 21-day dermal toxicity studies in the rabbit were considered for risk assessment. A no observed adverse effect level (NOAEL) of 90 mg/kg bw/day was established based on hyperactivity and inhibition of brain cholinesterase at 500 mg/kg bw/day. It should be noted that dermally, the effects were reversible following a recovery period. The target MOE selected when using these studies is 100, thus accounting for standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of these studies and MOE is considered to be protective of all populations including pregnant women and their unborn children.

Short-, Intermediate- and Long-term Inhalation Risk Assessment

To assess farmer M/L/A, custom M/L/A and postapplication workers

For short-, intermediate- and long-term inhalation risk assessment, there were no repeat-dose inhalation toxicity studies that assessed cholinesterase inhibition. Thus, the acute neurotoxicity study in rats was selected for risk assessment with the assumption that absorption via inhalation is equivalent to oral absorption. A NOAEL of 0.25 mg/kg bw/day was established based on brain cholinesterase inhibition at the next highest dose level. The lowest observed adverse effect level (LOAEL) is 0.5 mg/kg bw/day. A target MOE of 100 is required to account for standard uncertainty factors of 10-fold for inter-species extrapolation and 10-fold for intra-species variability. The selection of this study and MOE is considered to be protective of all populations including pregnant women and their unborn children.

Dermal Absorption

A dermal absorption value was not required for this assessment as dermal toxicity studies were selected for the dermal risk assessment.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to methomyl through mixing, loading or applying the pesticide and/or when entering a treated site to conduct activities such as scouting and/or handling of treated crops.

Mixer, Loader and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders and applicators. The following supported uses were assessed:

- mixing/loading solutions for application to forests and woodlands, greenhouse cucumbers, apples, broccoli, cabbage, cauliflower, Brussels sprouts, sweet corn, tomatoes, tobacco, canola, flax, oats, wheat, barley, peas, potatoes, snap beans, sweet corn, canola;
- mixing/loading wettable powder in water soluble packages for application to forests and woodlands, apples, broccoli, cabbage, cauliflower, Brussels sprouts, sweet corn, tomatoes, tobacco, canola, flax, oats, wheat, barley, peas, potatoes, snap beans, sweet corn, canola;
- loading granules for application to barns, poultry houses, kennels;
- groundboom application to broccoli, cabbage, cauliflower, Brussels sprouts, sweet corn, tomatoes, tobacco, canola, flax, oats, wheat, barley, peas, potatoes, snap beans, sweet corn, canola;
- airblast application to forests and woodlands, apples, tobacco;
- aerial application to canola, flax, oats, wheat, barley, canola;
- handwand application to forests and woodlands, greenhouse cucumbers;
- right-of-way sprayer application to forests and woodlands; and
- hand application of granules to barns, poultry houses, kennels.

Based on the number of applications, workers applying methomyl would generally have a short-term (up to 30 days) duration of exposure. The exception may be for greenhouse and structural uses of methomyl (e.g. heated barns, kennels or poultry houses), which could represent an intermediate (up to 6 months) to long-term (more than 6 months) duration of exposure. The PMRA estimated handler exposure based on the following level of personal protection:

- mid-level personal protective equipment (PPE): cotton coveralls over a long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves. PPE also includes a respirator where required.

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment may be refined with exposure data representative of modern application equipment and engineering controls. Biological monitoring data could also further refine the assessment.

No acceptable chemical-specific handler exposure data were submitted for methomyl; therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED), Version 1.1. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE. In most cases, the PHED did not contain appropriate data sets to estimate exposure to workers wearing a respirator or cotton coveralls. These was estimated by incorporating a 75% protection factor for cotton coveralls into the dermal unit exposure data or a 90% protection factor for a respirator into the inhalation unit exposure data.

Occupational risk estimates associated with applying, mixing and loading for current label uses meet the target MOE, provided mid-level PPE are used in all scenarios. A respirator was required while mixing/loading all solutions, mixing/loading wettable powder in water-soluble packages for aerial application, airblast application, right-of-way application and high-pressure handwand application.

Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers entering treated agricultural sites. Based on the methomyl use pattern, there is potential for short-term (<30 days) postapplication exposure to methomyl residues for workers, with the exception of people who work with greenhouse crops, which would have a longer duration of exposure.

Chemical-specific dislodgeable foliar residue (DFR) data and activity specific transfer coefficients (TC) were used to estimate postapplication exposure resulting from contact with treated foliage at various times after application. DFR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant to the skin of the worker. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late season corn) and reflect standard agricultural work clothing worn by adult workers. Postapplication exposure activities include harvesting, thinning, pruning, scouting and irrigating trees.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter a treated site. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE (i.e. >100 for short-term exposure scenarios).

Two grape and two sweet corn outdoor DFR studies were assessed for methomyl. All studies, with the exception of one grape DFR study were considered unacceptable for use in the postapplication assessment due to major limitations in the studies. As a result, the default peak DFR value of 20% of the application rate and a 10% dissipation rate per day was used for all outdoor crops, with the exception of apples which used data from the grape DFR study (peak DFR of 15% of the application rate with a dissipation rate of 14% per day).

Three greenhouse DFR studies were assessed for indoor uses of methomyl. All studies were considered to be unacceptable for use for the indoor postapplication assessment due to major limitations in the studies. A default peak DFR value of 20% of the application rate was used for all indoor crops. As there is no default dissipation rate for indoor scenarios, only exposure on the day of application could be assessed.

The postapplication risk estimates include a number of conservative inputs, such as the assumption that workers are exposed to residues following the maximum number of applications at the maximum rate.

Based on available data, to achieve the target MOEs for postapplication workers, REIs ranged from 0 to 2 days for the majority of the various postapplication scenarios. Longer REIs were

required for corn hand detasseling/harvesting (18 days) and apple tree thinning (5 days). Appendix V summarizes calculated REIs for selected postapplication activities, based on currently available exposure data, and the target MOE of 100.

At this time, there are insufficient data to assess postapplication exposure to greenhouse cucumbers. As MOEs did not reach the target MOE on day 0 and a dissipation rate could not be estimated, an REI could not be proposed. Additional data, as outlined below, is needed to refine the risk assessment.

There are also insufficient data to assess postapplication exposure to workers entering treated structures (e.g. barns, poultry houses and dog kennels) that have been treated with granular bait. It is anticipated that exposure is less than that for applicators; however, it cannot be adequately assessed. Mitigation by way of wearing chemical-resistant gloves while handling bait, used bait, treated surfaces or deceased insects is proposed. Additional data, as outlined below, could help to refine the risk assessment.

The assessments could be refined with the following data:

- DFR data including dissipation for greenhouse uses;
- enhanced information on the methomyl use pattern, including typical rates and the number of applications per season;
- survey information on critical worker activities that typically take place for each crop during the use season, and the timing of these activities with respect to crop growth and applications of methomyl, particularly with regards to corn and apple activities; and
- passive dosimetry, biological monitoring and additional DFR data.

With these additional data and information, it is expected that estimated exposure and risk would be more reflective of actual use.

3.2.3 Non-Occupational Exposure and Risk Assessment

Non-occupational risk assessment involves estimating risks to the general population, including children, during or after pesticide application. Currently no residential uses for methomyl are registered. However, there is potential for short-term exposure to adults and children during or immediately following commercial application of methomyl to trees in public parks.

At this time, there are insufficient data to quantitatively assess the risks to bystanders associated with non-occupational exposure from treated trees in parks. Additional data would be needed to quantify this exposure.

3.3 Dietary Risk Assessment

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for the *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods.

MRLs for methomyl are currently specified for some commodities (see Appendix IX). Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm.

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to methomyl from potentially treated imports is also included in the assessment. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by combining the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents the detailed acute and chronic risk assessments procedures.

Surveillance data representative of the national food supply were used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program. As well, data from the 2001 Market Basket Survey were also used.

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model–Food Commodity Intake Database (DEEM-FCID™, Version 2.03), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

For more information on the dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendix VI and VII.

3.3.1 Determination of Acute Reference Dose (ARfD)

To estimate acute dietary risk (1 day), the NOAEL of 0.25 mg/kg bw from the acute neurotoxicity study in rats was selected. This NOAEL was based upon inhibition of brain cholinesterase at the LOAEL of 0.5 mg/kg bw. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were used. The *Pest Control Products Act* factor was reduced to onefold for the reasons outlined in Section 3.1, under the *Pest Control Products Act* Hazard Characterization.

$$\text{ARfD} = \frac{0.25 \text{ mg/kg bw}}{100} = 0.0025 \text{ mg/kg bw}$$

3.3.2 Acute Dietary Exposure and Risk Assessment

Acute dietary risk was calculated considering the highest ingestion of methomyl that would be likely on any one day, and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of methomyl that might be consumed in one day. When the expected intake of residues is less than the acute reference dose (ARfD), then acute dietary exposure is considered to be acceptable.

Probabilistic acute dietary exposure analyses were performed to determine the exposure and risk estimates resulting from the use of methomyl on domestic and imported agricultural commodities.

The acute dietary risk (food only) for the Canadian population subgroups at the 99.9th percentile was above the level of concern of the PMRA. Risk estimates for the general population subgroup was approximately 113%. Exposure, relative to the reference dose, ranged from 89% for females 13 to 49 years to 410% for children 1 to 2 years. The major contributors were grapes and strawberries.

3.3.3 Determination of Acceptable Daily Intake (ADI)

To estimate dietary risk from repeat exposure, the acute neurotoxicity study in rats was selected for risk assessment. A NOAEL of 0.25 mg/kg bw was established based on brain cholinesterase inhibition at the next higher dose level (LOAEL = 0.5 mg/kg bw). The quick acting and reversible nature of cholinesterase inhibition with carbamates is considered as justification to default to the acute NOAEL that is lower than the subchronic or chronic NOAEL. In the case of methomyl, long-term daily exposures are considered as multiple daily exposures with each causing transient inhibition of cholinesterase with resulting potential toxicity. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were used. The *Pest Control Products Act* factor was reduced to onefold for the reasons outlined under the *Pest Control Products Act* Hazard Characterization Section.

$$\text{ADI} = \frac{0.25 \text{ mg/kg bw/day}}{100} = 0.0025 \text{ mg/kg bw/day}$$

3.3.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the acceptable daily intake (ADI). When the expected intake of residues is less than the ADI, then chronic dietary exposure is acceptable.

Deterministic chronic dietary exposure analyses were performed to determine the exposure and risk estimates resulting from the use of methomyl on domestic and imported agricultural commodities. As for the acute assessment, a large number of monitoring data were used. Field trial data were used when no monitoring data were available. Specific and empirical processing factors (DEEM™ defaults) as well as specific information regarding percentage of crop treated were incorporated to the greatest extent possible.

Deterministic chronic dietary exposure analyses were performed to determine the exposure and risk estimates that result from the use of methomyl on domestic and imported agricultural commodities, using a chronic reference dose (ADI) of 0.0025 mg/kg bw/day for all subpopulations. The chronic dietary (food only) exposure risk for all Canadian population subgroups is less than the reference dose and is, therefore, below the PMRA's level of concern. Risk estimates for the representative population subgroups were 2% for males 20 years and older, and 7% for the most affected population of children 1 to 2 years. Grape juice and sugarcane were MRLs identified as the major contributors to the risk estimate.

3.4 Exposure from Drinking Water

3.4.1 Concentrations in Drinking Water

Concentrations of methomyl in Canadian drinking water sources were modelled using the Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS) for surface water and the Leaching Estimation and Chemistry Model (LEACHM) for groundwater. Refined (Level 2) drinking water concentrations were estimated using crop-specific input parameters and reassessing the fate input parameters to choose less conservative values than in a previous Level 1 assessment. The modelling results indicate that methomyl has the potential to leach into groundwater and run-off to surface water.

Canadian monitoring data on methomyl are limited. The provincial and territorial governments along with Environment Canada and the Department of Fisheries and Oceans were contacted to request water monitoring data for methomyl. Only one dataset that included detections of methomyl was received. This dataset was from monitoring conducted in the 1980s and is, therefore, not considered current for this assessment. Methomyl has been detected in surface water and groundwater in the United States; therefore, there is qualitative evidence that methomyl can contaminate water resources. The chronic and acute estimated drinking water concentrations calculated from the exposure models were 65.9 µg/L and 63.4 µg/L, respectively.

See Appendix X for more details on concentrations in drinking water.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure was addressed by calculating drinking water levels of comparison (DWLOCs). DWLOCs can only be calculated if all other exposures are not of concern to the PMRA, as the DWLOC simply expresses the difference between the reference dose and the non-drinking water exposure. For this reason acute DWLOCs were not calculated. The DWLOC values were compared to model estimates of potential drinking water exposure.

The chronic DWLOC values ranged from 24 µg/L for the most sensitive subpopulation of infants to 86 µg/L for the general population.

The exposure estimates for drinking water exceeded the DWLOCs calculated for infants and children and are of concern.

For more information, please refer to Section 3.5, Aggregate Exposure and Risk Assessment.

3.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (i.e. oral, dermal and inhalation).

3.5.1 Aggregate Acute Risk and Exposure Assessment

Aggregate acute risk was not calculated as the risk determined from food exposure alone was above the level of concern.

3.5.2 Aggregate Chronic Risk and Exposure Assessment

Chronic aggregate exposure to methomyl is considered to arise from dietary and drinking water exposures only and is compared to the ADI. Residential exposure was not included in the aggregate assessment because a quantitative risk assessment was not conducted for possible bystander exposure. Chronic aggregate exposure from food and water is of concern, based on the model derived DWLOCs that showed that drinking water exposure estimates are above the PMRA's level of concern. As a result, aggregate chronic risk was not calculated.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Summary

Available fate data (see Appendix IX, Table 1) indicate methomyl is expected to be slightly or non-persistent in soil, depending on the soil type, and non-persistent in water. Methomyl is very soluble in water (58 g a.i./L) and is mobile in soil and is expected to leach to ground water. Methomyl is unlikely to bioaccumulate (log K_{ow} = 0.093). Phototransformation is not an important route of dissipation of Methomyl on soil (half-life [$t_{½}$] = 34 days), whereas

phototransformation in water is rapid ($t_{½}$ = 1 day), and is an important route to transformation under certain conditions. Aerobic biotransformation in soil occurs relatively rapidly ($t_{½}$ = 10–45 days).

Hydrolysis
Hydrolysis is not expected to be a major transformation route for methomyl in aquatic systems at pHs below 9 as minimal transformation occurred in the 30-day laboratory studies at these pHs. At pH 9, fifty percent hydrolysis required 30 days.

Phototransformation
Phototransformation of methomyl on soil is not an important route of transformation from the environment with a $t_{½}$ of 34 days. In surface waters phototransformation is expected to be an important route of transformation ($t_{½}$ = 1 day), depending on latitude, weather, and water depth.

Volatilization
A low vapour pressure (vp = 5.4×10^{-6} mm Hg at 25°C) and a Henry's law constant of 1.84×10^{-10} atm m^3/mol, ($1/H = 1.33 \times 10^{-8}$) suggests that volatilization from water is not likely to be a significant process contributing to the transformation of methomyl from the aquatic environment. This can also be said for moist soil.

Soil Biotransformation
Methomyl is transformed by microorganisms under both anaerobic and aerobic conditions. In aerobic soils methomyl was found to have first order $t_{1/2}$s ranging from 10–45 days, which would classify methomyl as non-persistent to slightly persistent, respectively. In anaerobic soils methomyl is non-persistent having a first order $t_{½}$ of 14 days.

Soil Mobility
Calculated organic-carbon partition coefficients (K_{oc}) ranging from 5–91 indicate that methomyl does not absorb to soil and thus can potentially be mobile. On the basis of soil thin layer chromatography studies, methomyl and its major transformation product, *S*-methyl-*N*-hydroxythioacetimidate, are classified as moderately mobile to mobile and moderately mobile to very mobile. Methomyl meets all of the criteria for leaching. In addition, the calculated groundwater ubiquity score is 3.96 which classifies methomyl as a leacher. Therefore, the PMRA concludes that methomyl has the potential to leach to groundwater. Methomyl's high solubility and mobility also indicate that it is likely to reach surface water sources via run-off.

Canadian Field Dissipation
No information is available on the field dissipation of methomyl in relevant ecozones; however, studies conducted in Mississippi and California reported in field dissipation times (DT_{50}) of 6 days and 54 days, respectively, which concurs with the laboratory data (although leaching likely contributed to rapid dissipation in Mississippi).

Aquatic Biotransformation
In water, aerobic biotransformation is the main route of transformation of methomyl ($t_{½}$ = 4.5 days in sediment:water systems).This classifies methomyl as non-persistent in water.

Due to its high solubility, low K_{oc}s (5–91) and low log K_{ow} (0.093), methomyl is likely to be in solution in aquatic environments rather then be adsorbed to dissolved or suspended organic matter in the water column and therefore likely susceptible to biotransformation in the water column.

Surface Water Monitoring

A search for methomyl water monitoring data in Canada revealed that routine analysis for methomyl is not conducted. American monitoring studies also confirm that methomyl can contaminate ground and surface waters. The rate of detection across states was highly variable, as were detection levels and measured concentrations. For example, the American National Contaminant Occurrence Database provided data on the detection of methomyl in public water systems in the United States. There were 33 detections of methomyl from a total of 32 156 samples analysed. A minimum detection of 0.1 µg/L was reported along with a maximum of 3.0 µg/L and mean of 1.34 µg/L.

Transformation Products

Methomyl undergoes full mineralization in soil, producing no major transformation products other than carbon dioxide (CO_2). In aquatic systems, mineralization also occurs; three major transformation products were detected, *S*-methyl-*N*-hydroxythioacetimidate, acetonitrile (an organic solvent, in sediment and volatile phase) and acetamide in sediment.

4.2 Effects on Non-Target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models that take into consideration the application rate(s), chemical properties and environmental fate properties, including the transformation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening-level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes

into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies and probabilistic risk-assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

A risk assessment of methomyl to terrestrial organisms was based upon an evaluation of toxicity data on bees (acute contact), earthworm (acute), two standard test species of birds (acute oral, dietary, and chronic; variety of formulations) as well as nine additional species of small song birds and five species of mammals (acute oral and chronic). A summary of terrestrial toxicity data for methomyl is presented in Appendix IX, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with methomyl (see Table 4 of Appendix IX).

Liquid Formulation

Invertebrates

For acute contact toxicity of methomyl to bees the lethal concentrations to 50% (LD_{50}) is 0.1 µg a.i./bee, equivalent to 0.112 kg a.i./ha. In comparison, the application rates of methomyl range from 0.27–1.94 kg a.i./ha. Therefore, there is a risk of bee mortality resulting from the direct exposure of bees to methomyl given that all application rates of methomyl are higher than the application rate that would result in 50% mortality of honeybees (RQ = 17.3). Based on information available from the United States Environmental Agency (USEPA) ecological effects database, non-target beneficial invertebrates, such as wasps, damsel bugs, etc., are also at risk from exposure to the insecticide based on the use pattern in Canada. Earthworms are at negligible risk of ecological effects following one application of methomyl (RQ = 0.06–0.4).

Birds

Birds can be exposed to methomyl through the consumption of contaminated food (e.g. seeds, insects, vegetation), as well as from drinking water and dermal contact. Because of the extensive research done on methomyl, nine small bird species acute toxicity endpoints were available. All small birds as well as the mallard duck and bobwhite quail are acutely sensitive to methomyl. The red-winged blackbird appears to be the most sensitive species. The least sensitive species is the rock dove. Dietary exposure to the test chemical resulted in somewhat lower sensitivity in five test species, compared to acute oral exposure. Upon chronic exposure via diet, a small but biological significant reduction in the numbers of eggs laid per hen and a subsequent reduction in the numbers of offspring were seen in bobwhite quail. A no observed effect concentration (NOEC) based on these reproduction effects of 150 mg a.i./kg was determined. Similarly in the mallard duck, chronic effects such as reduction in number of viable embryos were observed, having an NOEC of 150 mg a.i./kg diet.

Methomyl poses an acute risk to birds. At the higher application rates of methomyl, it takes less than one day of continuous feeding of contaminated food to reach the oral dose that resulted in

50% mortality in the laboratory studies. The screening level assessment (assuming that the birds consume 100% of their diet immediately after the final application within the treatment field) indicates that many bird species are at risk of acute adverse effects including mortality, particularly the small birds that frequent field crops and orchards. The most sensitive small bird was the house sparrow (RQ = 48). However, results provided by Environment Canada indicate that the acute risk to birds appears to be lower than that predicted by the screening level assessment. These results are based on models derived from field mortality monitoring and by incorporating oral toxicity and dermal toxicity. Field application models indicate avian mortality may occur in 2% of treated fields at the highest field application rate (970 g a.i./ha–lettuce). Orchard application models indicate that avian mortality is unlikely to occur in orchards.

Acute dietary exposure to methomyl presents a risk to wild birds such as the bobwhite quail, but does not present a risk to the mallard duck. Similarly, a chronic risk was identified for the bobwhite quail based on a screening level assumption of 100% contaminated food consumption. Given that methomyl is not persistent in the environment (foliage half-life = 3 days) and birds are not likely to feed only in treated fields for a prolonged period of time, the identified risk for chronic exposure is likely to be overestimated.

Mammals

Mammals can be exposed to methomyl through consumption of contaminated food (e.g. vegetation, insects, seeds, etc.). All mammals that were tested are acutely sensitive to methomyl exposure, but are less sensitive to prolonged low-dose exposure or chronic effects. This screening level assessment indicates a risk of mammalian mortality following the application of methomyl, with less than one day of continuous feeding on a contaminated diet to reach the oral dose resulting in 50% mortality of the laboratory animals. Based on the acute toxicity values and using the standard PMRA scenario, the level of concern was exceeded for acute dietary exposure (RQ = 99) at all application rates, even from a single application. Taking into consideration the dietary preference and daily consumption rates, it was concluded that the level of concern was exceeded for small mammals on a chronic dietary basis (RQ = 18) only at the high treatment rate used in orchards. Given methomyl is not persistent in the environment and wild mammals are not likely to remain in the area of treatment, the level of risk determined is likely overestimated; therefore, the PMRA concludes that a risk of chronic effects on mammals from exposure to methomyl is minimal.

Refined Assessment

Given that the LOC at the screening level assessment was exceeded for birds and mammals, a refined assessment was also conducted. This determines the risk to birds and mammals that will be exposed to pesticide drift in areas adjacent to sites of application. As a result, the application rate (or the rate at which the non-target organisms will be exposed) was determined taking into consideration the percentage drift which is expected to be deposited 1 m downwind from the edge of the spray equipment. The percentage of spray drifts used in this assessment were 6% for ground spray equipment and 60% for aerial spray equipment. Using this approach, the assessment indicated that birds and small mammals are at risk of adverse effects when exposed to off-site drift that will occur during ground and aerial application of methomyl. Risk mitigation measures will be explored.

Appendix IX, Tables 4 and 6, summarizes the risk assessment for methomyl for terrestrial organisms.

Granular Formulation

Methomyl granular formulations are used as a fly bait and are scattered in areas where flies congregate at an application rate of 2.5 g a.i./100 m^2 or 87 500 granules/100 m^2. In the current assessment it was assumed that birds will not be attracted to the methomyl granules as a food source, but may use it as a grit source; thus, the assessment compared the number of granules that would be required to reach the LD_{50} of five bird species (northern bobwhite quail, mallard duck, rock dove, house sparrow and red-winged blackbird). Based on the application rate, there would be enough granules available for consumption to reach the LD_{50} of all the bird species considered. Upon consideration of data investigating the number of granules present in the gizzard of the bird species the mallard duck is the only species that has the potential to consume enough methomyl granules to reach the LD_{50}. Given the use pattern, it is unlikely that mallard ducks and similar bird species would be in the areas where methomyl is applied in order to consume this large amount of product. Methomyl is applied in and around feedlots, dairies, stables, broiler houses, hog houses, livestock barns and kennels, on walkways in caged poultry houses and around outside areas of dog pens or runways. Therefore, the risk to birds from exposure to granule methomyl is considered low.

Mammals can be exposed to granular pesticides through ingestion of food with granules attached (i.e. an earthworm or an insect that has granules attached to it), dermal contact, inhalation and inadvertent ingestion of granules as food (i.e. mistaking granules for seeds). The use pattern of the granules could potentially allow for exposure of wild mammals to the granules. However, the granular formulations contain a formulant that would deter the consumption of the granules by mammals; therefore, it is unlikely that the mammals will consume the number of granules required to reach the LD_{50}.

4.2.2 Effects on Aquatic Organisms

Risk to aquatic organisms is based on an evaluation of toxicity data on methomyl for fifteen freshwater species (six invertebrate; nine fish) and six Estuarine/marine species (five invertebrate; one fish). A summary of aquatic toxicity data for methomyl is presented in Appendix IX, Table 3. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with methomyl (see Appendix IX, Table 5). For the screening level scenario, EECs were determined based on the overspray of an 80 cm deep body of water for fish and invertebrate assessments; a 15 cm depth was used to estimate risk to amphibians. These water depths are also used in the refined assessments of drift and runoff. It should be noted that methomyl is expected to be in aquatic systems near treated areas for more than 20 days (based on the water/sediment dissipation rate) where three applications can be used with a 5–7 day application interval. Therefore, chronic toxicity is also expected in the case of invertebrates and subchronic toxicity for early life stages of fish. Where appropriate, buffer zones are calculated using the chronic toxicity endpoint.

Fish, Amphibians and Invertebrates

All of the aquatic organisms are acutely sensitive to methomyl, while invertebrates are more sensitive to toxic effects than fish. Among invertebrate taxa, emergent insects and pelagic invertebrates are sensitive to carbamate insecticides, while benthic invertebrates such as worms and bivalves are resistant. The screening level assessment for aquatic organisms indicates the levels of concern were exceeded for freshwater invertebrates at all application rates (RQ = 30 acute; 1064 chronic), while for fish the LOC was exceeded for all but the lowest single application rate (RQ = 1.5–8). The LOC was exceeded for amphibians for acute and chronic effects. Although no amphibian data was available, effects were estimated from fish toxicity data (1/10 lethal concentration to 50% (LC_{50}), acute; early life stage test, chronic) (RQ = 42 acute; 40 chronic). Estuarine/marine invertebrates are at risk (except bivalves), having RQs of 1.7–44.8, but the single marine fish species tested showed resistance. Thus, the marine fish LOC is not exceeded.

Refined Assessment

As the level of concern for aquatic organisms was exceeded in several instances a refined assessment was conducted which considers exposure from run-off and drift (see Appendix IX, Tables 6 and 7).

Drift

The potential for effects on freshwater organisms resulting from drift were examined by determining the percentage of the application rate that would be required to reach the threshold of effects for freshwater invertebrates and fish. As indicated by the percentage of the application rate required to reach the threshold of effects for invertebrates (0.5%–4.2% for three species all single application rates) and fish (8.7% for Atlantic salmon at the highest single application rate; higher values required for other species and lower rates), spray drift of methomyl into aquatic environments poses a risk to freshwater invertebrates and some species of fish, depending on the application rate.

In addition, to assess the risk from drift, the water EECs were re-calculated assuming drift was the sole contributor to the resulting EEC. For ground application, it was assumed that 6% of the application will drift, and for aerial application, it was assumed that 60% of the application will drift. These percentages were used to determine the amount of methomyl in a body of water that was a result of drift from an application adjacent to the body of water. The calculated RQs indicate that the LOC was exceeded for invertebrates at all rates for aerial application and all but the lowest application rate for ground. For fish, drift from ground application did not result in a risk, but aerial application did result in risk (RQ = 4.8) with the exception of the lowest application rate. Risk to amphibian species was predicted from aerial and ground application, (RQ = 2.6–26).

The LOCs for marine invertebrates were exceeded (RQ = 27) at all treatment rates from exposure to aerial spray drift, a similar situation was determined for ground application (RQ = 2.7), however, no risk is predicted at the lowest rate. A drift deposit of less than 2% of the application rate is required to reach threshold effects for marine invertebrates, indicating a risk.

Runoff

To assess the risk of exposure to methomyl via runoff, refined EECs were predicted using the PRZM/EXAMS model. The values determined using the model include the 90th percentile of the yearly peak, yearly 96-hours, 21-days, 60-days, 90-days and yearly average values. Using the appropriate EECs with the available toxicity data, the risk quotients indicate that the LOC is exceeded for both invertebrates and fish from exposure to runoff. For freshwater invertebrates, the endpoints used in the risk assessment were 14.3 µg a.i./L (½ 96-hours LC_{50}) for the acute assessment and the 21-days NOEC of 0.4 µg a.i./L for the chronic assessment. The calculated risk quotients (5.7–145) indicate the acute and chronic threshold of effects for aquatic invertebrates were exceeded. Thus, freshwater invertebrates are at risk from concentrations resulting from runoff. Although freshwater fish are less sensitive to methomyl, the LOC is still exceeded from runoff (1–1.5) based on acute and early-life stage toxicity. Marine/estuarine invertebrates are also at risk, (RQ of 8.6). There are no risks determined for marine fish.

5.0 Value

5.1 Commercial and Restricted Class Products

5.1.1 Commercial and Restricted Class Uses for Which Information on the Value of Methomyl is Sought

Appendix II lists all the uses of methomyl the registrant continues to support.

The PMRA welcomes feedback on the availability and extent of use of chemical alternatives to methomyl for the uses listed in Appendix II and information regarding the availability, effectiveness and extent of use of non-chemical pest management practices for any of the registered uses of methomyl. This information will allow the PMRA to better understand sustainable pest-management options.

5.2 Domestic Class Products

There are no registered Domestic Class methomyl products.

5.3 Value of Methomyl

Some uses of methomyl may require further discussion concerning their value. These concerns may relate to economics, quarantine pests and/or the lack of viable alternatives for uses with risk concerns or for uses that are not supported by the registrant, etc. Uses for which the loss of methomyl would be detrimental are discussed below.

5.3.1 Systemic Mode of Action

Methomyl is effective in two ways:

- as a contact insecticide, killing target insects upon direct contact; and
- as an insecticide that works as a stomach poison, killing target insects upon ingestion of treated plants.

Methomyl is a systemic insecticide; the active ingredient is absorbed and transported throughout the plant, imparting protection to the entire plant. Systemic insecticides are effective against insects with piercing-sucking mouthparts, such as aphids and thrips, as the systemic insecticide moves within the vascular tissues where aphids feed and into cells where thrips feed.

As a systemic insecticide that acts upon ingestion, methomyl is effective for the control of pests that otherwise could not be targeted with contact insecticides or non-systemic insecticides that act as a stomach poison, for example:

- chewing insects once they enter the host plants: corn earworm and European corn borer larvae bore into the midrib of the leaf and migrate into the stalk of the plant or husk of the ear; and

- insects, such as thrips, beet armyworm and slugs, that hide within the developing plant leaves while feeding and are protected from direct contact with insecticidal sprays.

Systemic insecticides have greater flexibility of application timing than non-systemic and contact insecticides for the control of pests that feed internally upon the host. Contact insecticides and non-systemic insecticides that act by ingestion are limited to controlling pests that feed from within the host prior to their entry into the host (e.g. corn earworm, European corn borer). The application timing must be precise to target the majority of the pest population prior to entry into the host. Non-systemic insecticides with a prolonged period of residual activity or repeated applications of insecticides with short residual activity may therefore be required to replace one application with a systemic active ingredient.

5.3.2 Methomyl Uses Identified With Limited Registered or Viable Alternatives, or For Which the Systemic Mode of Action Has Value

In the following Table, the PMRA identifies detailed information on the potential value of methomyl use.

Table 1 The Potential Value of Methomyl

Methomyl uses to control internal feeding pests; uses for which there are no registered alternatives; and uses for which the availability of viable alternatives is either limited or currently under re-evaluation are listed below.

Crop	Pest	Registered Alternatives[1] (MoA)[2]	Comments
Brussels sprouts Strawberry	Slugs	(Other): ferric phosphate, ferric sodium ethylene diamine tetra-acetic acid, metaldehyde (strawberry only)	**Application method:** Ferric phosphate, ferric sodium EDTA and metaldehyde are formulated as a bait. Methomyl is a spray treatment, which is more effective than baits when alternative food sources are available such as when the crop is mature. **This use was registered through the User Requested Minor Use Label Expansion (URMULE) program.**
Canola	Beet webworm	(1B): trichlorfon, (3): deltamethrin	**No viable alternative active ingredient (Eastern Canada):** Trichlorfon is not a viable alternative as it is currently under re-evaluation and the food uses are not supported by the registrant. Deltamethrin is the only viable alternative to methomyl for canola grown in the Prairie provinces and Peace River region of British Columbia. Deltamethrin is not registered for control of beet webworm in Eastern Canada. **Resistance management (Western Canada):** Methomyl is a Mode of Action (MoA) resistance group 1A insecticide. Deltamethrin is a MoA resistance group 3 insecticide. Methomyl is required for rotation with deltamethrin for the purposes of delaying the development of resistance.
	Alfalfa looper	(1B): chlorpyrifos	**Registered alternative active ingredient is currently under re-evaluation.**

Crop	Pest	Registered Alternatives[1] (MoA)[2]	Comments
Corn (sweet)	Aphids	(1A): pirimicarb (2A): endosulfan (Other): insecticidal soap	**Systemic mode of action is important to control the pest.** **Lack of viable registered alternative active ingredients.** Endosulfan is currently under re-evaluation. The preliminary risk assessment for endosulfan indicates a level of concern for workers and the environment. Pirimicarb is not a viable alternative, as its use is not supported by the registrant as a result of re-evaluation. Use of pirimicarb on sweet corn will expire 31 December 2009. Due to the short residual activity and the potential for phytotoxicity from repeated applications insecticidal soap is not considered a viable alternative. **This use of methomyl was registered through the URMULE program.**
	European corn borer	(1A): carbaryl, carbofuran (1B): acephate, trichlorfon (Quebec only) (3): lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin (5): spinosad (11): *Bacillus thuringiensis* var *kurstaki*	**Systemic mode of action is important to control the pest.** European corn borer feeds on all parts of the plant, however the greatest economic damage is incurred when borers feed on the ears of the corn plant. Of the registered alternative active ingredients to methomyl for the control of European corn borer on sweet corn, acephate and carbofuran are systemic insecticides. Carbaryl is only slightly systemic. All three are currently under re-evaluation.

Crop	Pest	Registered Alternatives[1] (MoA)[2]	Comments
	Corn earworm	(1A): carbaryl (2A): endosulfan (3): lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin	**Systemic mode of action is important to control the pest.** Corn earworm feed at the tip of the cob and move down the ear as they grow. Feeding is almost always confined to the top third of the ear. Although corn earworm damages only a small percentage of the kernels, its presence and droppings are very distasteful to most consumers. Methomyl is the only active ingredient registered to control corn earworm on sweet corn having an effective systemic mode of action. Of the registered alternative active ingredients to methomyl for the control of corn earworm, carbaryl is slightly systemic. Endosulfan and the synthetic pyrethroids are non-systemic insecticides.
Flax	Flax bollworm	None	**No registered alternative active ingredients.**
	Bertha armyworm	(1B): chlorpyrifos, trichlorfon	**Registered alternative ingredients are currently under re-evaluation.** Chlorpyrifos is currently under re-evaluation. Trichlorfon is not a viable alternative as it is currently under re-evaluation and the food uses are not supported by the registrant.

Crop	Pest	Registered Alternatives[1] (MoA)[2]	Comments
Green-house cucumber	Western flower thrips	(4): nicotine	**Resistance management:** The only registered alternative to methomyl for the control of western flower thrips on greenhouse cucumbers is nicotine, a MoA group 4 insecticide. Methomyl (MoA resistance group 1A) is required for rotation with nicotine for the purpose of delaying the development of resistance. **Systemic mode of action is important to control the pest.** This pest is difficult to target with contact insecticides as it feeds within buds, leaves and other enclosed parts of the plant. **This use was registered through the URMULE program.**

Crop	Pest	Registered Alternatives[1] (MoA)[2]	Comments
Lettuce	Beet army worm	(1A): carbaryl (1B): diazinon, trichlorfon	**Systemic mode of action is important to control the pest.** The beet armyworm, *Spodoptera exigua*, can be a very destructive pest of lettuce. Serious economic damage may occur after cupping. Beet armyworm larvae enter the lettuce heads from the bottom of the plant and feed inward. Often damage can not be seen without removing frame leaves and dissecting the head. All the registered alternative active ingredients to methomyl for use to control armyworm on lettuce are currently under re-evaluation. Trichlorfon is not a viable alternative to methomyl as food uses are not supported by the technical registrant. Diazinon is proposed to be phased out. As this pest feeds within the host, a systemic mode of action is required for effective control being as a surface spray application with a contact insecticide will not target the pest. Of the registered alternative active ingredients to methomyl, only carbaryl is slightly systemic.
Peas	Alfalfa looper	(1B): carbaryl, naled	**There is a limited number of viable registered alternatives.** The re-evaluation of naled was completed in 2006. Naled is registered for use on peas for processing only. Carbaryl is currently under re-evaluation.

Crop	Pest	Registered Alternatives[1] (MoA)[2]	Comments
Wheat, oats, barley	Thrips	(1B): dimethoate	**Registered alternative active ingredient is currently under re-evaluation.**

[1] This is a list of registered options only as of April 2008. Health Canada does not endorse any of the options listed. The registration status of active ingredients under re-evaluation may change pending the final regulatory decision.

[2] Insecticide and Acaricide Resistance Management Group Numbers based on DIR 99-06 *Voluntary Pesticide Resistance Management Labelling based on Target Site/Mode of Action*: 1A = acetylcholinesterase inhibitors (carbamates); 1B = acetylcholinesterase inhibitors (organophosphates); 2A = gamma-aminobutyric acid (GABA)-gated chloride channel antagonists; 3 = sodium channel modulators; 4 = acetylcholine receptor agonists/antagonists (nicotine); 5 = acetylcholine receptor modulators (spinosyns); 11 = microbial disruptors of insect mid-gut membranes

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's TSMP, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, methomyl was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of methomyl were also considered, including transformation products formed in the environment, and contaminants and formulants in the technical product and the end-use product. Methomyl and its transformation products were evaluated against the following Track 1 criteria: persistence in soil ≥182 days; persistence in water ≥182 days; persistence in sediment ≥365 days; persistence in air ≥2 days; bioaccumulation log K_{ow} ≥5 or bioconcentration factor ≥5000 (or bioaccumulation factor ≥5000). In order for methomyl or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The technical product and end-use product, including formulants, were assessed against the contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern, Part 3 Contaminants of Health or Environmental Concern. The PMRA has reached the following conclusions.

- Methomyl is not bioaccumulative. The log *n*-octanol–water partition coefficient (log K_{ow}) is 0.093.

- Methomyl does not meet the criteria for persistence as its half-life values in water (up to 5 days) and soil (up to 45 days) are below the TSMP Track 1 cut-off criteria.
- No data were provided for persistence of methomyl in air; however, it is not volatile.
- The major transformation products carbon dioxide, S-methyl-*N*-hydroxythioacetimidate, acetamide and acetonitrile do not meet TSMP Track 1 criteria.
- End-use products of methomyl do not contain any Track 1 formulants.
- Methomyl does not contain any Track 1 microcontaminants.

The use of methomyl is not expected to result in the entry of TSMP Track 1 substances into the environment.

7.0 Summary of the Preliminary Risk Assessment and Consultation

The preliminary risk assessment for methomyl, conducted with the information available to the PMRA at this time, indicates a level of concern for health (e.g. dietary and drinking water exposure) and the environment. Additional use pattern information (percent crop treated, area treated per day, number of applications, rates, etc.) and any other relevant data will be considered to determine if the evaluations presented in this document can be refined. The PMRA is soliciting the public and all interested parties to submit information that may be used to refine these assessments and/or mitigate health and environmental risks as well as comments on the value of methomyl for specific uses. The PMRA will review all information received, revise the risk assessments as necessary and provide a regulatory proposal in a future Proposed Re-evaluation Decision.

The following confirmatory data would be required to support the continued registration of methomyl and to support any expansion of methomyl use.

- A developmental neurotoxicity study (data code [DACO] 4.5.14) with assessment of cholinesterase activities in the maternal animals and offspring or a comparative cholinesterase study.

8.0 Additional Data

The following studies were identified as gaps in the database or may be needed to support certain uses or to reduce the mitigation measures required. The list is provided for information and may be revised as a result of updated assessment for the Published Proposed Re-Evaluation Decision.

8.1 Data Related to Health Risk Assessment

8.1.1 Data Related to Toxicological Exposure

•	DACO 4.3.6 or 4.3.7	A short-term inhalation study
•	DACO 4.2.5	A dermal irritation study

8.1.2 Data Related to Occupational Exposure

Greenhouse Crops

•	DACO 5.6/5.7	Postapplication: passive dosimetry data or biological monitoring data for performing re-entry tasks on cucumbers in greenhouses following application of methomyl
•	DACO 5.9	Dislodgeable residues: data for dislodgeable residues of methomyl on greenhouse cucumbers to establish appropriate REIs
•	DACO 5.10	Air monitoring data or rationale for a waiver

Structures Treated with Granular Bait

•	DACO 5.2	Additional information on postapplication activities in these areas following application of granular bait
•	DACO 5.6/5.7	Postapplication: passive dosimetry data or biological monitoring data for performing re-entry tasks in treated barns, poultry houses and dog kennels following application of methomyl granular bait
•	DACO 5.10	Air monitoring data or rationale for a waiver

Sweet Corn

•	DACO 5.9	Dislodgeable residues: data for dislodgeable residues of methomyl on corn or rationale for acceptable REI for hand detasseling or hand harvesting at the preharvest interval (PHI).

Re-entry Exposure in Public Parks

•	DACO 5.2	Additional information on this use scenario that could be used to help characterize potential exposure to bystanders in the park. This might include information such as application method, frequency of use, types of trees and potential for bystander contact, etc.

- DACO 5.6/5.7 — Postapplication: passive dosimetry data or biological monitoring data for bystanders re-entering parks with trees treated with methomyl.

8.1.3 Data Related to the Dietary Exposure

- DACO 6.2 — Animal metabolism study
- DACO 6.3 — Plant metabolism study
- DACO 7.2 — Analytical methodology
- DACO 7.2.1 — Supervised residue trial analytical methodology
- DACO 7.2.2 — Enforcement analytical methodology
- DACO 7.2.3 — Inter-laboratory analytical methodology validation
- DACO 7.2.4 — Multi-residue analytical methodology evaluation
- DACO 7.2.5 — Storage stability of working solution
- DACO 7.3 — Freezer storage stability data
- DACO 7.4 — Crop residue data
- DACO 7.4.1 — Supervised residue trial study
- DACO 7.4.2 — Residue decline study
- DACO 7.4.3 — Confined crop rotation trial study
- DACO 7.4.4 — Field crop rotation trial study
- DACO 7.4.5 — Processed food
- DACO 7.4.6 — Residue data for crops used as livestock feed
- DACO 7.5 — Livestock, poultry, egg and milk residue data

Drinking water surveillance data may be required to confirm the results of the exposure and risk assessments.

8.2 Data Related to Environmental Risk Assessment

Additional field studies may be required to refine risk assessment for aquatic invertebrates.

List of Abbreviations

↑	increase
↓	decrease
♂	male
♀	female
^{14}C	Carbon 14
°C	degree(s) Celsius
AD	administered dose
ADI	acceptable daily intake
a.i.	active ingredient
A	applicators
amu	atomic mass unit(s)
ARD	Acute reference dose
ARfD	acute reference dose
ASAE	American Society of Agricultural Engineers
BChE	brain cholinesterase
bw	body weight
cm	centimetre(s)
cm^2	centimetre(s) square
CMRR	Canadian Maximum Registered Rate
CAF	composite assessment factor
CO_2	carbon dioxide
CAS	Chemical Abstracts Service
CDN	Canadian
CFIA	Canadian Food Inspection Agency
ChE	cholinesterase
CHO	Chinese hamster ovary cells
d	day(s)
DACO	data code
DER	data evaluation report
DFR	dislodgeable foliar residue
DEEM™	Dietary Exposure Evaluation Model
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50%
DWLOC	drinking water levels of comparison
EC_{50}	effective concentration on 50% of the population
EChE	erythocyte cholinesterase
EDTA	ethylene diamine tetra-acetic acid
EEC	environmental exposure concentration
F_0	parental generation
F_1	first filial generation
F_2	second filial generation
FOB	functional observational battery
FPD-S	flame photometric detector with a sulfur filter
g	gram(s)
GC	gas chromatography

GI	gastrointestinal
GLC	gas liquid chromatography
GR	granular
Gran	granular fertilizer
hrs	hour(s)
ha	hectare(s)
HCT	hematocrit
HGB	hemoglobin
hp	high pressure
HPLC	high pressure liquid chromatography
hr(s)	hour(s)
HGPRT	hypoxanthine-guanine phosphoribosyl transferase
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting of Pesticide Residues
K_d	adsorption coefficient
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol–water partition coefficient
km	kilometre(s)
L	litre(s)
lp	low pressure
LEACHM	Leaching Estimation and Chemistry Model
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
m	metre(s)
M	molar
m^2	metre(s) square
m^3	metre(s) cube
mg	milligram(s)
M/L	mixers/loaders
mm Hg	millimetre(s) of Mercury
mL	millilitre(s)
min	minutes
mM	millimolar
MML	methomyl
MOE	margin of exposure
mol	mole
MRL	maximum residue limit(s)
MTDB	maximum theoretical dietary burden
N/A	not applicable or not available
NCOD	National Contaminant Occurrence Database (United States)
ng	nanogram(s)
nm	nanometre(s)
NOEL	no observed effect level
NOAEL	no observed adverse effect level

NOEC	no observed effect concentration
N/S	not stated
NZW	New Zealand White
^{32}P	phosphorus 32
Pa	pascal(s)
PAM	pesticide analytical manual
PCPA	*Pest Control Products Act*
PChE	plasma cholinesterase
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	part per million
PRVD	Proposed Re-evaluation Decision
PRZM/EXAMS	Pesticide Root Zone Model/Exposure Analysis Modeling System
RBC	red blood cells
RCG	residue chemistry guidelines
RED	re-registration decision
REI	restricted entry interval
REV	Re-evaluation Note
R_f-value	retention time value
ROW	right of way
RQ	risk quotient
SD	standard deviation
SMC	sulphur microcoulometric detector
SD	Sprague Dawley
SN	solution
SP	soluble powder
$t_{½}$	half-life
TC	transfer coefficient
TL_{50}	toxic level 50%
TLC	thin layer chromatography
TRN	(Z)-9-tricosene
TRR	total radioactive residues
TSMP	Toxic Substances Management Policy
µgCi	microCurrie(s)
µg	microgram(s)
UDS	unscheduled DNA synthesis
URMULE	user requested minor use label expansion program
USC	use site category
USEPA	United States Environmental Protection Agency
UV	ultraviolet
vp	vapour pressure
wk	week
WSP	wettable powder in water-soluble packages
wt(s)	weight(s)

Appendix I Registered Methomyl Products as of 26 March 2008[1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee[2]
19139	Technical	E.I. Du Pont Canada Company	Methomyl Technical Insecticide	Solid	MML: 98.7%
10868	Restricted	E.I. Du Pont Canada Company	Lannate Insecticide Toss-N-Go	Soluble Powder	MML: 90%
11725	Commercial	E.I. Du Pont Canada Company	Lannate L Insecticide	Solution	MML: 215 g a.i./L
15176	Commercial	Wellmark International	Starbar Premium Fly Bait	Granular	MML: 1% TRN: 0.025%
24969	Commercial	Troy Biosciences Inc.	Stimukil Fly Bait	Granular	MML: 1% TRN: 0.025%
25358	Commercial	Farnam Companies Inc.	Blue Streak Fly Bait	Granular	MML: 1% TRN: 0.025%

1 Excluding discontinued products or products with a submission for discontinuation.

2 MML: methomyl; TRN: (z)-9-tricosene.

Appendix II Registered Commercial and Restricted Class Uses of Methomyl in Canada as of 26 March 2008

Site(s)	Pest(s)	Formulation Type[1]	Application Methods and Equipment	Product Rate	Active Ingredient Rate[2] (kg a.i./ha)	Maximum Number of Applications per Year	Min Interval Between Applications (day)	Supported Use?[3]
Use-Site Category 4: Forest and Woodlots								
Balsam fir and spruce in Christmas tree plantations, farm woodlots, municipal parks, rights-of-way	Spruce budworm	Soluble Powder	Conventional ground equipment: hydraulic sprayers, mist blowers, airblast sprayers	270–540 g/ha	0.24–0.49	2	3	Y
		Solution		1.25–2.25 L/ha	0.27–0.48			
Use-site Category 5: Greenhouse Food Crops								
Greenhouse cucumbers	Western flower thrips	Solution	Hydraulic sprayers, backpack sprayer	22 mL of formulated product/ 100L	4.7 g/100L	3	5	Y, M
Use-site Category 14: Terrestrial Food Crops								
Apple	Obliquebanded leafroller	Soluble Powder	Conventional ground equipment: air blast sprayer hydraulic sprayers	1.6 kg/ha	1.44	2	14	Y, M
		Solution		6.75 L/ha	1.45			
	Mullein leaf bug	Soluble Powder		1.6 kg/ha	1.44	1	Not applicable	
		Solution		6.75 L/ha	1.45			
	Apple aphids	Soluble Powder		1–2.1 kg/ha	0.90–1.89	3 (at high rate) Not specified (low rate)	5	Y
	Codling moth	Soluble Powder		540 g/ha–2.1 kg/ha	0.49–1.89			
	Spotted tentiform leafminer (1st generation)	Soluble Powder		1.6–2.1 kg/ha	1.44–1.89			
		Solution		6.75–9.0 L/ha	1.45–1.94			

Site(s)	Pest(s)	Formulation Type[1]	Application Methods and Equipment	Product Rate	Active Ingredient Rate[2] (kg a.i./ha)	Maximum Number of Applications per Year	Min Interval Between Applications (day)	Supported Use?[3]
	White apple leafhopper	Soluble Powder		1.4 kg/ha	1.26			
		Solution		6 L/ha	1.29			
	Winter moth	Soluble Powder		0.6 kg/ha	0.54			
		Solution		2.5 L/ha	0.54			
Broccoli, Brussels sprouts, cabbage	Cabbage looper, imported cabbageworm, diamondback moth	Soluble Powder	Conventional ground equipment: hydraulic sprayers	270–540 g/ha	0.24–0.49	3 (at high rate) Not specified (low rate)	5	Y
		Solution		1.25–2.25	0.27–0.48			
Brussels sprouts	Slugs (larvae of grey garden slug)	Soluble Powder		775 g/ha	0.7	1	Not applicable	Y, M
		Solution		3.25 L/ha	0.7			
Cauliflower	Cabbage looper, imported cabbageworm, diamondback moth	Soluble Powder		270–540 g/ha	0.24–0.49	3 (at high rate) Not specified (low rate)	5	Y
Lettuce (field)	Cabbage looper, beet armyworm	Soluble Powder		510 g/ha–1 kg/ha	0.46–0.90	3 (at high rate) Not specified (low rate)	5	Y
	Cabbage looper, larmyworm	Solution		2.25–4.5 L/ha	0.48–0.97			
Canola	Alfalfa looper, bertha armyworm, beet webworm, clover cutworm	Soluble Powder	Conventional ground equipment: hydraulic sprayers Conventional aerial application equipment.	216–510 g/ha	0.19–0.46	3 (at high rate) Not specified (low rate)	5	Y
		Solution		0.9–1.25 L/ha	0.19–0.27			
Flax	Bertha armyworm	Soluble Powder		220–270 g/ha	0.20–0.24	3 (at high rate) Not specified (low rate)	5	Y
	Bertha armyworm, flax bollworm	Solution		0.9–1.25 L/ha	0.19–0.27			

Site(s)	Pest(s)	Formulation Type[1]	Application Methods and Equipment	Product Rate	Active Ingredient Rate[2] (kg a.i./ha)	Maximum Number of Applications per Year	Min Interval Between Applications (day)	Supported Use?[3]
Barley, oats, wheat	Common armyworm	Soluble Powder		270–540 g/ha	0.24–0.49	3 (at high rate) Not specified (low rate)	5	Y
		Solution		1.25–2.25 L/ha	0.27–0.48			
	Thrips	Soluble Powder		300 g/ha	0.27	Not specified		
		Solution		1.25 L/ha	0.27			
Peas	Alfalfa looper, pea aphid	Soluble Powder	Conventional ground equipment: hydraulic sprayers	510 g/ha	0.46	Not specified	5	Y
		Solution		2.25 L/ha	0.48			
Potatoes	Leafhoppers, fleabeetles, aphids	Soluble Powder		540 g/ha	0.49	Not specified	5	Y
		Solution		2.25 L/ha	0.48			
	variegated cutworm	Soluble Powder		270–540 g/ha	0.24–0.49	3 (at high rate) Not specified (low rate)		
		Solution		1.25–2.25 L/ha	0.27–0.48			
Snap beans	European corn borer	Soluble Powder		550 g/ha	0.5	Not specified	3	Y, M
		Solution		2.3 L/ha	0.5			
Strawberries	Slugs (larvae of grey garden slugs	Soluble Powder		775 g/ha	0.7	1	Not applicable	Y, M
		Solution		3.25 L/ha	0.7			
Sweet corn	Aphids	Soluble Powder		430–620 g/ha	0.39–0.56	3	5	Y, M
		Solution		1.8–2.6 L/ha	0.39–0.56			
	Corn earworm	Soluble Powder		430–625 g/ha	0.39–0.56	4	2	Y
		Solution		1.8–2.6 L/ha	0.39–0.56			
	European corn borer	Soluble Powder		625 g/ha	0.56	Not specified	5	
		Solution		2.6 L/ha	0.56			
Tobacco	Tomato hornworm, aphids	Soluble Powder		540 g/ha	0.49	Not specified	5	Y
		Solution		2.25 L/ha	0.48			

Site(s)	Pest(s)	Formulation Type[1]	Application Methods and Equipment	Product Rate	Active Ingredient Rate[2] (kg a.i./ha)	Maximum Number of Applications per Year	Min Interval Between Applications (day)	Supported Use?[3]
Tomatoes	Tomato fruitworm, aphids, variegated cutworm	Soluble Powder		270–540 g/ha	0.24–0.49	3 (at high rate)	5	Y
		Solution		1.25–2.25 L/ha	0.27–0.48	Not specified (low rate)		
Use-site Category 20: Structural								
Farm buildings (feedlots, dairies, stables, hog houses, livestock barns), kennels and poultry houses (broiler and caged layer houses)	Blow fly, eye gnat, flesh fly, house fly, little house fly, flies (general)	Granular	Shaker can/ bait station	250 g/ 100m^2	2.5 g /100m^2	daily (365)	1	Y

1 The active ingredient rate is listed in kg a.i./ha unless the rate is specified as a concentration (i.e. g a.i./volume of spray) or as g a.i./100m^2.

2 Y = use is supported by the registrant; and M = use was registered as a URMULE.

Appendix III Toxicology Profile for Methomyl

NOTE: Depression of plasma cholinesterase (PChE) is not considered by the PMRA to be a toxicologically adverse effect; it can be viewed as a marker of exposure. Depression of erythocyte cholinesterase (EChE) can be viewed as a surrogate for adverse changes in the peripheral nervous tissue in acute and some short-term studies. In studies of longer duration, depression of EChE is also not considered by the PMRA to be a toxicologically adverse effect.

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Table 1 Toxicology Profile for Methomyl

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism/Toxicokinetic Studies			
Absorption, distribution, metabolism and excretion studies – Sprague Dawley rats Rats Cynomolgus ♂ monkeys	Oral administration		**Absorption**: Rapidly absorbed via G.I. tract. **Distribution**: Following a single dose, ~8–9% in rat body and 4–5% in monkey body at 7 days. Following repeat-dosing, ~10% retained in rat body after 24 hrs. Methomyl found in blood, liver, fat, and kidney but does not accumulate. **Metabolism**: The syn-isomer gives rise to an oxime that is metabolized primarily to CO_2 while the anti-isomer primarily produces acetonitrile. In the rat there is some conversion of the syn- to anti-isomer. Metabolites: In rats, the major urinary metabolite is mercapturic acid derivative of Methomyl (18% of AD), in air ~22–23% of AD is $^{14}CO_2$, ~12–13% of AD is ^{14}C-acetonitrile. In monkeys, in air ~31–38% of AD is $^{14}CO_2$ and ~4–7% is ^{14}C-acetonitrile. >10 additional minor urinary metabolites found in rats including acetonitrile, acetate, a sulfate conjug ate of Methomyl oxime and acetamide. There are three metabolic pathways: • displacement of the *S*-methyl moiety with endogenous glutathione, which is subsequently further metabolized by enzymatic cleavage to the corresponding mercapturic derivative; • cleavage of the carbamate ester releasing Methomyloxime which then may be rapidly metabolized or conjugated; • in vivo isomerization of syn-Methomyl to the anti-isomer which upon hydrolysis produces anti-Methomyloxime; this metabolite may then undergo a Beckman rearrangement and elimination reaction to form acetonitrile. **Excretion**: Single dose in rats: ~50% urine, 35% expired air. Repeat dose in rats: ~30% urine, 50% expired air

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
		Single dose in monkeys: ~24–35% urine, 40% expired air. Very little in feces (2–3%) in either species or dose regime. Near complete excretion within 24 hrs. Elimination half-life in rats ~5 hrs.	
Acute Toxicity Studies			
Acute oral toxicity – rats	>98% purity	LD_{50} = 17–34/23.5–30 mg/kg bw (♂/♀) Clinical signs included tremors, low posture and salivation **High toxicity**	
Acute oral toxicity – chickens	>98% purity	LD_{50} = 28 mg/kg bw (♀) **High toxicity**	
Acute oral toxicity – rabbits	>98% purity	LD_{50} = 30 mg/kg bw (♂) **High toxicity**	
Acute oral toxicity – dogs	>98% purity	LD_{50} = 20 mg/kg bw **High toxicity**	
Acute oral toxicity – monkeys	Purity – N/S	LD_{50} = 40 mg/kg bw **High toxicity**	
Acute dermal toxicity – rats	>98% purity	LD_{50} >1000 mg/kg bw (♂) **Slight toxicity**	
Acute dermal toxicity – rabbits	>98% purity	LD_{50} >2000 mg/kg bw Clinical signs included miosis, decreased motor activity, diarrhea, salivation and breathing difficulties **Low toxicity**	
Acute inhalation toxicity – rats	Purity N/S	LC_{50} = 0.26 mg/L Clinical signs included exaggerated breathing, reduced respiration, tremors, hypersensitivity, exophthalmus, piloerection and staggering **Moderate toxicity**	
Acute dermal irritation – rabbits	>98% purity	**Non-irritating**	
Acute eye irritation – rabbits	Purity N/S	**Non-irritating** (only 10 mg used; cholinergic signs including miosis, incoordination, tremors, convulsions, salivation, lethargy and rales during first hour); 15 mg (92.4% pure) in the eye of a ♀ rabbit caused cholinergic symptoms and death after 20 min. **High toxicity via ocular exposure**	
Skin sensitization – guinea pigs	98% purity	**No sensitization potential** in Buehler assay	

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Subchronic Toxicity Studies			
90-day oral toxicity – Charles River rats 10/sex/group	100% purity 0, 10, 50, 250 ppm in diet (~0, 0.5, 2.5, 12.5 mg/kg bw/day); one group fed 125 ppm (~6.25 mg/kg bw/day) for 6 wks and 500 ppm (~25 mg/kg bw/day) for remainder	6.25	12.5 mg/kg bw/day: Slight ↓ bw and ↓ food consumption; moderate erythroid hyperplasia in bone marrow (♂). No inhibition of ChE in any treated group.
90-day oral toxicity – Fisher F344 rats 20/sex/group	>95% purity 0, 250, 790 or 2500 ppm in diet (= 0, 16/18, 58/57, or 243/187 ♂/♀ mg/kg bw/day)	16/18 (LOAEL)	≥ 16/18 mg/kg bw/day: ↑ number of thyroidal follicles lined by cuboidal to columnar cells, ↓ glucose, ↓ BChE (slight); ↓ bw, ↑ spleen weight, ↓ Hgb, ↓ RBC (♂); ↑ urogenital staining, ↓ hematocrit (♀) ≥ 58/57 mg/kg bw/day: ↓ BChE; ↑ urogenital staining, ↓ water intake, ↓ hematocrit (♂); ↑ spleen weight, ↓ Hgb, ↓ RBC (♀) 243/187 mg/kg bw/day: ↑ EChE, congestion and capsular thickening of spleen; ↑ food intake (♂); lacrimation, bw, ↓ water intake, ↓ uterine wall thickness (♀)
21-day dermal toxicity – NZW rabbits 10/sex/group, except 5/sex/mid-dose	98.35% purity 0, 5, 50, 500 mg/kg bw/day (5/sex in control and high-dose allowed to recover for 14 days)	50	≥ 50 mg/kg bw/day: ↓ PChE (♂) 500 mg/kg bw/day: ↑ hyperactivity, ↓ BChE, ↓ EChE (slight); ↓ PChE (♀) No effects observed on dermal irritation, hematology, clinical chemistry, organ weights or histopathology. All ChE returned to normal by end of recovery period.
21-day dermal toxicity – NZW rabbits 6/sex/group	98.6% purity 0, 15, 30, 45 or 90 mg/kg bw/day	90	No effects on ChE Note: No assessment of hematology, clinical chemistry, organ weights or histopathology.

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Neurotoxicity Studies			
Acute delayed neurotoxicity – hens	Purity N/S 28 mg/kg bw/day without atropine and 60–200 mg/kg bw/day under atropine protection		Salivation, lacrimation and some convulsions in survivors but no paralysis or neuropathology observed. **No evidence of delayed neurotoxicity.**
Acute oral neurotoxicity – rats 52/sex/group	98.6% purity 0, 0.25, 0.5, 0.75 or 2.0 mg/kg bw by gavage	0.25	All effects at 30 minutes postdosing unless specified ≥0.5 mg/kg bw: ↓ BChE; ↓ EChE (♀)≥0.75 mg/kg bw: ↓ PChE 2.0 mg/kg bw: tremors; ↓ weight gain between day 2–8 (♀) All ChE activity normal by 24 hrs postdosing
Cholinesterase reversibility – rats 40/sex/group	98.6% purity 0 or 3 mg/kg bw by gavage		3 mg/kg bw: tremors and ↓ BChE, ↓ EChE at 30 minutes postdosing Recovery by 2 hrs postdosing
28-day oral toxicity Sprague Dawley rats 8/sex/group	Purity N/S 0, 100, 400, 800 ppm in diet (~0, 5, 20, or 40 mg/kg bw/day)	20	40 mg/kg bw/day: ↓ BChE (♀) Note : Considered supplemental due to study limitations
Subchronic oral neurotoxicity – rats 42/sex/group incl. 10/sex/dose sacrificed at weeks 4 and 8	Purity N/S 0, 20, 50, 150 or 1500 ppm in diet for 91 days (~0, 1, 2.5, 7.5 or 75 mg/kg bw/day)	7.5	75 mg/kg bw/day: ↓ weight gain, ↓ food intake, tremors (particularly in first 4 wks), FOB observations of ↑ resistance to handling, ptosis and absent pupillary response, marginal inhibition of BChE
Chronic Toxicity/Oncogenicity Studies			
2-year chronic toxicity/ oncogenicity – Sprague Dawley rats 80/sex/group including 10/sex/group for 52-week sacrifice, additional 20/sex/group for ChE activity	>99% purity 0, 50, 100, 400 ppm in diet (= 0, 2.4/3.2, 4.8/6.3, 19.9/26.2 mg/kg bw/day, ♂/♀)	4.8/6.3	19.9/26.2 mg/kg bw/day: ↓ weight gain; ↑ bone marrow hyperplasia, ↑ focal degeneration/angiectasis in adrenal cortex, ↑ focal hyperplasia in adrenal medulla (♂); ↓ Hgb, ↓ RBC, ↓ hematocrit (♀) **No evidence of carcinogenicity.** Note: Study inadequate for ChE assessment

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
22-month chronic toxicity/ oncogenicity – Charles River rats 35/sex/group	Purity N/S 0, 50, 100, 200 or 400 ppm in diet (~ 0, 2.5, 5, 10 or 20 mg/kg bw/day)	5	≥10 mg/kg bw/day: ↓ Hgb after 18 months, ↑ extramedullary hematopoiesis of spleen (♀). 20 mg/kg bw/day: ↑ renal tubular hypertrophy, vacuolation and inhibition of protein in cytoplasm in proximal tubule; ↓ weight gain, ↑ relative testes weight (♂); protein in lumen of kidney (♀) **No evidence of carcinogenicity** Note: considered supplemental due to study limitations
104-week oncogenicity – CD-1 mice 80/sex/group	>99% purity 0, 50, 100 (reduced to 75 ppm at wk 39) or 800 ppm in diet (reduced to 400 ppm at wk 28 and to 200 ppm at wk 39) (≈ 0, 8.7/10.6, 15.3/19.1, 93.3/118.5 mg/kg bw/day, ♂/♀)	8.7/10.6	>8.7/10.6 mg/kg bw/day: ↑ food intake ≥15.3/19.1 mg/kg bw/day: ↓ red cell mass (↓ Hgb, ↓ RBC, ↓ hematocrit) at week 13 and 26; ↑ mortality by week 26 (♀) 93.3/118.5 mg/kg bw/day: ↑ mortality; ↑adrenal wt (♂) **No evidence of carcinogenicity.**
2-year chronic toxicity – Beagle dogs 4/sex/group incl. 1/sex/group for 52 week sacrifice	90% purity 0, 50, 100, 400 or 1000 ppm in diet (~0, 1.25, 2.5, 10 or 25 mg/kg bw/day)	2.5	≥10.0 mg/kg bw/day: swollen/irregular epithelial cells of proximal convoluted tubules with ↑ pigment, ↑ pigmentation of spleen (♂) 25.0 mg/kg bw/day: 2/4 ♂ exhibited cholinergic effects during week 13, 1 ♀ died at wk 9, replacement ♀ died on day 18 exhibiting convulsive seizures, ↑ bile duct proliferation, ↑ extramedullary hematopoiesis of spleen, ↑hematopoiesis in bone marrow activity, ↓ HgB, ↓ RBC, ↓ hematocrit
Reproductive and Developmental Toxicity Studies			
Developmental toxicity – Charles River rats 25♀/group	>99% purity 0, 50, 100 or 400 ppm in diet (≈ 0, 4.9, 9.4 or 33.9 mg/kg bw/day) on days 6–15 of gestation	Maternal = 9.4 Developmental = 33.9	**Maternal:** 33.9 mg/kg bw/day: ↓ bw gain, ↓ food consumption **Developmental:** No effects noted **No evidence of teratogenicity.**

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Developmental toxicity – Sprague Dawley rats 22♀/group	Purity N/S 0, 1.0, 3.5 or 15 mg/kg bw/day on days 6–15 of gestation by gavage	Maternal = 1.0 Developmental = 3.5	**Maternal:** ≥3.5 mg/kg bw/day: ↓ bw gain, ↓ food consumption 15 mg/kg bw/day: mortality, salivation, tremors **Developmental:** 15 mg/kg bw/day: ↓ fetal weight, ↓ crown rump length, ↑malformations (situs inversus), ↑ variations (14th rib, bilateral unossified metacarpals)
Developmental toxicity – NZW rabbits 20♀/group	98.7% purity 0, 2, 6 or 16 mg/kg bw/day on days 7–19 of gestation by gavage	Maternal = 6.0 Developmental = 16	**Maternal:** 16 mg/kg bw/day: clinical signs (tremors, hyperactivity, body jerks, salivation, convulsions, ataxia), mortality (1–3 days after dosing). **Developmental:** No effects noted **No evidence of teratogenicity.**
Developmental toxicity – NZW rabbits 20♀/group	Purity – N/S 0, 2, 8 or 32 mg/kg bw/day on days 7–19 of gestation by gavage	Maternal = 8.0 Developmental = 8	**Maternal:** 32 mg/kg bw/day: clinical signs (tremors, salivation, pupillary constriction), mortality, ↓ weight gain, ↓ uterine weight **Developmental:** 32 mg/kg bw/day: ↑ variations (13 thoracic vertebrae, bilateral lumbar ribs)
Reproductive toxicity – Sprague-Dawley rats 13♂ and 26♀/group in F_0; 20♂ and 40♀/group in F_1 (2-generation)	>98% purity 0, 75, 600 or 1200 ppm in diet (= 0, 5/5, 37/39 or 74/76 mg/kg bw/day F_0 ♂/♀, 0, 7/7, 56/59 or 117/128 mg/kg bw/day F_1 ♂/♀)	Parental and Offspring LOAEL = 5 Reproductive NOAEL = 5	**Parental**: ≥5–7 mg/kg bw/day: slight ↓ bw gain pre-mating and during gestation (F_1); ↑ body tics (F_0 ♂) ≥37–59 mg/kg bw/day: ↓ bw gain pre-mating and during gestation (F_0), ↓ food intake (F_1/F_2); ↓ Hgb, RBC and Hct, ↑ body tics (F_0 ♀) 74–128 mg/kg bw/day: clinical signs (F_0) including hyperactivity (♂/♀), abnormal gait, piloerection (♂), confusion, hyperexcitability, tremors (♀) **Reproductive:** ≥37–59 mg/kg bw/day: ↓ birth weight (F_1/F_2) 74–128 mg/kg bw/day: ↑ stillborn (F_2) **Offspring**: ≥5–7 mg/kg bw/day: ↓ bw at day 14 and 21 only (F_1) ≥37–59 mg/kg bw/day: ↓ bw gain (F_1/F_2) 74–128 mg/kg bw/day: ↓ viability index (F_1/F_2), ↓ lactation index (F_1)

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Genotoxicity Studies			
Gene mutation *S. typhimurium* TA 100, TA 1535, TA1537, TA 1538 *E. coli* WP2 uvrA	Purity – technical 1–1000 ug/plate with and without activation	Negative	
Gene mutation *S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538	Purity – technical 0.005–50 mM with and without activation	Negative	
Gene mutation CHO cells, HGPRT	99% purity 10–55 mM without activation, 100–350 mM with activation	Negative	
Gene mutation CHO V79 cells	Purity N/S 1–10 mM with and without activation	Negative	
Sex-linked recessive lethal – *D. melanogaster*	Purity – technical 4 and 10 mg/kg	Negative.	
In vitro assays – human lymphocytes (whole blood cultures)	Purity – technical Doses ranging from 0.01–2 mM	Negative for sister chromatid exchange, DNA single-strand breaks and DNA oxidative damage; positive for chromosome aberrations and micronuclei	
Micronucleus test CHO cells	Purity N/S 2–32 mg/L	Positive	
Micronucleus test – mice	Purity N/S 6 mg/kg bw	Positive	
Micronucleus test – mice	Purity N/S 12 mg/kg bw	Negative.	
Micronucleus test – mice	Purity N/S 10 mg/kg bw	Negative.	
Micronucleus test – rats	99% purity 2–20 mg/kg bw	Negative.	
Unscheduled DNA synthesis – rat hepatocytes	99% purity 1–75 000 µM	Negative.	

Study/Species/ # of animals per Group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Unscheduled DNA synthesis – WI38 human fibroblasts	Purity – technical 10^{-3}– 10^{-7} M with and without activation	Negative	
DNA repair assay – *E. coli, B. subtilis*	Purity – technical 1 mg/disc	Negative.	
In vivo DNA damage – mice	Purity N/S 5 mg/kg bw	Positive for single-strand breaks in liver and kidney measured by alkaline elution assay. Positive for oxidative damage in liver measured by 8-OH-guanosine formation. Negative for DNA adduct formation in liver measured by ^{32}P post labelling assay.	

Appendix IV Toxicology Endpoints for Health Risk Assessment for Methomyl

Table 1 Toxicology Endpoints for Use in Health Risk Assessment for Methomyl

EXPOSURE SCENARIO	ENDPOINT	STUDY	DOSE (mg/kg bw/day)	CAF or MOE[a]
Acute Dietary	Cholinesterase inhibition	Acute rat neurotoxicity	0.25	100
	ARfD = 0.0025 mg/kg bw			
Chronic Dietary	Cholinesterase inhibition	Acute rat neurotoxicity	0.25	100
	ADI = 0.0025 mg/kg bw/day			
Short-, Intermediate- and Long-Term[b] Dermal	Cholinesterase inhibition	21-day dermal rabbit toxicity (two studies)	90	100
Short-, Intermediate- and Long-Term[c] Inhalation[c]	Cholinesterase inhibition	Acute rat neurotoxicity	0.25	100

[a] Composite assessment factor (CAF) refers to total of uncertainty and *Pest Control Products Act* factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments

[b] Relevant for all durations of exposure.

[c] As an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation.

Appendix V Occupational and Residential Exposure Risk Estimates for Methomyl

Table 1 Occupational Mixer, Loader and Applicator Exposure and Risk Assessment with Mid-Level PPE

Crop	Method of Application	Form	Rate[a] kg a.i./ha	Area Treated[b] ha/day	Daily Exposure µg/kg bw/day		Margins of Exposure (MOE)		
					Dermal[c]	Inhalation[d]	Dermal[e]	Inhalation[f]	Combined[g]
Use-Site Category 4: Forests and Woodlands									
Balsam fir, spruce in xmas tree plantations, woodlots, parks, rights-of-way (For high pressure handwand, 1000 L of water used per hectare)	ROW sprayer	WSP	0.49	75	279	0.36	322	700	**221**
	Airblast			50	173	0.27	519	940	**334**
	Backpack			3	43	1.3	1650	192	**172**
	Lp handwand			3	15	0.95	5829	263	**252**
	Hp handwand			3750 L	64	0.4	1397	631	**435**
Balsam fir, spruce in Christmas tree plantations, woodlots, parks, rights-of-way (For high pressure handwand, 1000 L of water used per hectare)	ROW sprayer	SN	0.48	75	286	0.34	314	737	**220**
	Airblast			50	178	0.25	504	985	**333**
	Backpack			3	53	1.28	1685	196	**175**
	Lp handwand			3	15	0.93	5951	269	**257**
	Hp handwand			3750 L	63	0.39	1427	644	**444**
Use-Site Category 5: Greenhouse Crops									
Cucumbers (Rate and area treated are expressed in litres)	Backpack	SN	5×10^{-5} kg a.i./L	150 L	0.26	0.006	344 084	39 972	**35812**
	Lp handwand			150 L	0.07	0.005	1 215 442	54 917	**52543**
	Hp handwand			3750 L	6	0.38	14 569	658	**629**

Crop	Method of Application	Form	Rate[a] kg a.i./ha	Area Treated[b] ha/day	Daily Exposure µg/kg bw/day		Margins of Exposure (MOE)		
					Dermal[c]	Inhalation[d]	Dermal[e]	Inhalation[f]	Combined[g]
Use-Site Category 14: Terrestrial Food Crops									
Apples	Airblast	WSP	1.89	16	214	0.32	420	761	**271**
		SN	1.94		231	0.33	390	762	**258**
Broccoli, cabbage, cauliflower	Groundboom	WSP	0.49	30	6	0.24	14 799	1044	**975**
		SN	0.48		11	0.23	8130	1085	**957**
Brussel sprouts	Groundboom	WSP	0.7	16	5	0.18	19 479	1375	**1284**
		SN			9	0.18	10 453	1395	**1231**
Sweet corn	Groundboom	WSP	0.56	100	23	0.91	3885	274	**256**
		SN			43	0.9	2091	279	**246**
Tomatoes	Groundboom	WSP	0.49	30	6	0.24	14 799	1044	**975**
		SN	0.48		11	0.23	8130	1085	**957**
Tobacco	Airblast	WSP	0.49	16	56	0.67	1622	373	**303**
		SN	0.48		57	0.65	1576	382	**308**
	Groundboom	WSP	0.49	100	20	0.8	4440	313	**293**
		SN	0.48		37	0.77	2439	326	**287**
Canola	Aerial – M/L	WSP	0.46	400	21	0.47	4323	528	**471**
		SN	0.27		51	0.25	1780	1013	**645**
	Aerial – A	WSP	0.46		19	0.18	4829	1359	**1060**
		SN	0.27		11	0.11	8228	2315	**1807**
	Groundboom	WSP	0.46	100	19	0.75	4729	334	**312**
		SN	0.27		21	0.43	4336	579	**511**
Flax	Aerial – M/L	WSP	0.24	400	11	0.25	8286	1013	**902**
		SN	0.27		51	0.25	1780	1013	**645**
	Aerial – A	WSP	0.24		10	0.1	9256	2604	**2032**
		SN	0.27		11	0.11	8228	2315	**1807**
	Groundboom	WSP	0.24	100	10	0.39	9064	640	**597**
		SN	0.27		21	0.43	4336	579	**511**

Crop	Method of Application	Form	Rate[a] kg a.i./ha	Area Treated[b] ha/day	Daily Exposure µg/kg bw/day		Margins of Exposure (MOE)		
					Dermal[c]	Inhalation[d]	Dermal[e]	Inhalation[f]	Combined[g]
Oats, wheat, barley	Aerial – M/L	WSP	0.49	400	22	0.5	4058	496	**442**
		SN	0.48		90	0.44	1001	570	**363**
	Aerial – A	WSP	0.49		20	0.2	4534	1276	**995**
		SN	0.48		19	0.19	4628	1302	**1016**
	Groundboom	WSP	0.49	100	20	0.8	4440	313	**293**
		SN	0.48		37	0.8	2439	326	**287**
Use-Site Category 20 – Structural									
Barns, poultry houses	Hand	GR	0.25	0.4	79	0.87	1135	289	**230**

ROW = right of way; WSP = wettable powder in water-soluble packages; SN = solution; GR = granular; Lp = low pressure; Hp = high pressure, M/L = mixer/loader; A = applicator

[a] Maximum label rate

[b] Based on default assumptions and crop specific data. Where indicated, volumes used as opposed to areas treated per day are shown in litres.

[c] Where dermal exposure µg/kg bw/day = (unit exposure × area treated × rate)/70 kg bw

[d] Where inhalation exposure µg/kg bw/day = (unit exposure × area treated × rate)/70 kg bw

[e] Based on a NOAEL of 90.0 mg/kg bw/day from a dermal study; target MOE = 100

[f] Based on a NOAEL of 0.25 mg/kg bw/day from an oral study; Target MOE = 100

[g] Combined MOE = 1 /(1/MOE_D + 1/MOE_I); target MOE = 100.

Table 2 Occupational Mixer, Loader and Applicator Exposure and Risk Assessment for Custom Applicators with Mid-Level PPE

Crop	Method of Application	Form	Rate[a] kg a.i./ha	Area Treated[b] ha/day	Daily Exposure[b] µg/kg/day		Margins of Exposure		
					Dermal[c]	Inhalation[d]	Dermal[e]	Inhalation[f]	Combined[g]
USC 14: Terrestrial Food Crops									
Peas	Groundboom	WSP	0.46	300	57	2.29	1576	111	**104**
		SN	0.48		111	2.3	813	109	**96**
Potatoes	Groundboom	WSP	0.49	300	61	2.39	1480	104	**98**
		SN	0.48		111	2.3	813	109	**96**
Snap beans	Groundboom	WSP	0.5	300	61	2.41	1465	103	**97**
		SN			114	2.37	788	105	**93**
Sweet corn	Groundboom	WSP	0.56	200	46	1.82	1942	137	**128**
		SN	0.48		74	1.53	1220	163	**144**

Crop	Method of Application	Form	Rate[a] kg a.i./ha	Area Treated[b] ha/day	Daily Exposure[h] µg/kg/day		Margins of Exposure		
					Dermal[c]	Inhalation[d]	Dermal[e]	Inhalation[f]	Combined[g]
Canola	Aerial M/L	WSP	0.46	400	21	0.47	4323	528	**471**
		SN	0.27		51	0.25	1780	1013	**645**
	Aerial A	WSP	0.46		19	0.18	4829	1359	**1060**
		SN	0.27		11	0.11	8228	2315	**1807**
Canola	Groundboom	SN	0.27	300	62	1.3	1445	193	**170**
		WSP	0.46		57	2.25	1579	111	**104**
Flax	Aerial M/L	WSP	0.24	400	11	0.25	8286	1013	**902**
		SN	0.27		52	0.25	1780	1013	**645**
	Aerial A	WSP	0.24		10	0.1	9256	2604	**2032**
		SN	0.27		11	0.11	8228	2315	**1807**
	Groundboom	WSP	0.24	300	30	1.17	3021	213	**199**
		SN	0.27		62	1.3	1445	193	**170**
Oats, wheat, barley	Aerial M/L	WSP	0.49	400	22	0.5	4058	496	**442**
		SN	0.48		90	0.44	1001	570	**363**
	Aerial A	WSP	0.49		20	0.2	4534	1276	**995**
		SN	0.48		19	0.19	4628	1302	**1016**
	Groundboom	WSP	0.49	300	61	2.39	1480	104	**98**
		SN	0.48		111	2.3	813	109	**96**

ROW = right of way; WSP = wettable powder in water-soluble packages; SN = solution, Lp = low pressure, hp = high pressure, M/L = mixer/loader; A = applicator

[a] Maximum label rate

[b] Based on default assumptions and crop specific data. Where indicated, volumes used as opposed to areas treated per day are shown in litres.

[c] Where dermal exposure µg/kg bw/day = (unit exposure × area treated × rate)/70 kg bw

[d] Where inhalation exposure µg/kg bw/day = (unit exposure × area treated × rate)/70 kg bw

[e] Based on a NOAEL of 90.0 mg/kg bw/day from a dermal study; target MOE = 100

[f] Based on a NOAEL of 0.25 mg/kg bw/day from an oral study; Target MOE = 100

[g] Combined MOE = $1/(1/MOE_D + 1/MOE_I)$; target MOE = 100.

Table 3 Occupational Postapplication Exposure Risk Estimates

Crop	Number of Applications	Minimum Interval (days) Between Applications	Activity	Transfer Coefficient[a] cm^2/hr	DFR[b] $\mu g/cm^2$	Dermal Exposure[c] µg/kg bw/day	MOE[d]	Proposed REI (days)
User-Site Category 4: Forests and Woodlands								
Balsam fir, spruce, woodlots, municipal parks, rights-of-ways rate: 0.49 kg a.i./ha (WSP) and 0.48 kg a.i./ha (SN)	2	3–4	Hand pruning, scouting, pinching, tying, training	500	1.6944 1.3997	96.82 79.98	930 1125	0
			Irrigating	1100	1.6944 1.3997	213.01 175.96	423 511	0
			Weeding, propping	100	1.6944 1.3997	19.36 16.00	4648 5623	0
User-Site Category 14: Terrestrial Food Crops								
Flax rate: 0.24 (WSP) and 0.27 (SN) kg a.i./ha	3	5–7	Irrigating, scouting	1500	0.9308 1.0472	159.57 179.51	564 501	0
			Harvesting	2000	0.7539 0.8482	172.33 193.87	522 464	0
Oats, rye, barley rate: 0.49 (WSP) and 0.48 (SN) kg a.i./ha	3	5–7	Irrigating	1500	1.9004 1.8616	325.78 319.13	276 282	0
			Scouting	100	1.9004 1.8616	21.72 21.28	4144 4230	0
Snapbeans rate: 0.495 kg a.i./ha	3 (not specified)	3–7	Irrigating, scouting	1500	2.2378	383.63	235	0
			Hand harvest	2500	2.2378	639.38	141	0
			Hand weeding	100	2.2378	25.58	3519	0
Broccoli, cabbage, cauliflower rate: 0.49 (WSP) and 0.48 (SN) kg a.i./ha	3	5–7	Hand pruning, hand harvest	5000	1.5393 1.5079	879.61 861.66	102 104	2
			Scouting	4000	1.9004 1.8616	868.75 851.02	104 106	0
			Weeding, thinning, irrigation	2000	1.9004 1.8616	434.37 425.51	207 212	0

Crop	Number of Applications	Minimum Interval (days) Between Applications	Activity	Transfer Coefficient[a] cm^2/hr	DFR[b] $\mu g/cm^2$	Dermal Exposure[c] µg/kg bw/day	MOE[d]	Proposed REI (days)
Brussel sprouts rate: 0.70 kg a.i./ha	1	N/A	Hand pruning, hand harvest	5000	1.4	800	113	0
			Scouting, w[illegible]ng, [illegible]ming, irrigation	2000	1.4	320	281	0
Lettuce rate: 0.90 (WSP) and 0.97 (SN) kg a.i./ha	3	5–7	Hand harvest, hand pruning, thinning	2500	3.1415 3.0472	897.56 870.63	100 103	1 2
			Irrigating, scouting	1500	3.4905 3.7620	598.37 644.91	150 140	0
			Hand weeding	500	3.4905 3.7620	199.46 214.97	451 419	0
Sweet corn rate: 0.56 kg a.i./ha	4	2–4	Irrigating, scouting, hand weeding	1000	3.1611	361.27	249	0
			Detasseling	17000	0.4326	840.53	107	18
Potatoes rate: 0.49 (WSP) and 0.48 (SN) kg a.i./ha	3	5–7	Irrigating, scouting	1500	1.9004 1.8616	325.78 319.13	276 282	0
			Hand weeding	300	1.9004 1.8616	65.16 63.83	1381 1406	0
Strawberries rate: 0.698 (WSP) and 0.70 (SN) kg a.i./ha	1	N/A	Hand harvest, pinch, prune, train	1500	1.3960 1.4000	239.31 240.00	376 375	0
			Irrigate, weed, scout, thin	400	1.3960 1.4000	63.82 64.00	1410 1406	0
Peas rate: 0.46 (WSP) and 0.48 (SN) kg a.i./ha	3	5–7	Irrigating, scouting	1500	1.7840 1.8616	305.83 319.13	294 282	0
			Hand harvest	2500	1.7840 1.8616	509.72 531.89	177 169	0
			Thinning	100	1.7840 1.8616	20.39 21.28	4414 4230	0

Crop	Number of Applications	Minimum Interval (days) Between Applications	Activity	Transfer Coefficient[a] cm^2/hr	DFR[b] $\mu g/cm^2$	Dermal Exposure[c] µg/kg bw/day	MOE[d]	Proposed REI (days)
Apples rate: 1.89 (WSP) and 1.94 (SN) kg a.i./ha	3	5–7	Thinning	3000	2.3436 2.4056	803.52 824.77	112 109	5
			Harvest, propping, pruning, training	1500	3.6910 3.7886	632.74 649.47	142 139	0
			Weeding, irrigation, scouting	500	3.6910 3.7886	421.82 432.98	213 208	0
Tomatoes rate: 0.49 (WSP) and 0.48 (SN) kg a.i./ha	3	5–7	Hand harvest, prune, stake, thin, train, tie	1000	1.9004 1.8616	217.19 212.75	414 423	0
			Irrigate, scout	700	1.9004 1.8616	152.03 148.93	592 604	0
			Weed	500	1.9004 1.8616	108.59 106.38	829 846	0
Canola rate: 0.46 (WSP) and 0.27 (SN) kg a.i./ha	3	5–7	Scouting	1500	1.7840 1.0472	305.83 179.51	294 501	0
Tobacco rate: 0.48 (WSP) and 0.49 (SN) kg a.i./ha	Repeat as necessary (Assumed: 3 apps)	5–7	Stripping, topping, hand: prune, weed, harvest	2000	1.8616 1.9004	425.51 434.37	212 207	0
			weeding, scouting, thinning	100	1.8616 1.9004	21.28 21.72	4130 4144	0
User-Site Category 5: Greenhouse Crops – Tier 1 Risk Assessment								
Greenhouse cucumbers rate: 0.50 kg a.i./ha	1	N/A	Re-entry tasks Day 0 exposure	7000	1.9392	1551.33	58	N/A

[a] WSP = wettable powder in water – soluble packages; SN = solution. Transfer coefficient defaults were used.

[b] DFR residues on the day where the MOE is greater than the target MOE (100).

[c] Dermal exposure = DFR × TC × 8 hr / 70 kg.

[d] Based on the short and intermediate term NOAEL of 90.0 mg/kg bw/day from a dermal study; target MOE = 100

N/A not applicable

MOEs that are below the target MOE are shaded.

Appendix VI Dietary Exposure and Risk Estimates for Methomyl

Table 1 Acute Dietary Exposures and Risk Estimates for Methomyl

Population	Acute	
	Exposure (mg/kg bw/day)	%ARfD
Canadian population	0.00282	**113**
All infants (<1 year)	0.004423	**117**
Children 1–2 yrs	0.010241	**410**
Children 3–5 yrs	0.006949	**278**
Children 6–12 yrs	0.00355	**142**
Youth 13–19 yrs	0.002046	82
Adults 20–49 yrs	0.002094	84
Adults 50+ yrs	0.002109	84
Females 13–49 yrs	0.002236	89

Table 2 Chronic Dietary Exposures and Risk Estimates for Methomyl

Population	Chronic		
	Exposure (mg/kg bw/day)	%ADI	DWLOC
Canadian population	0.000062	3	85
All infants (<1 year)	0.000091	4	**24**
Children 1–2 yrs	0.000179	7	**28**
Children 3–5 yrs	0.00016	6	**35**
Children 6–12 yrs	0.000104	4	**47**
Youth 13–19 yrs	0.000053	2	86
Adults 20–49 yrs	0.000045	2	86
Adults 50+ yrs	0.000045	2	86
Females 13–49 yrs	0.000047	2	76

Appendix VII Food Residue Chemistry Summary

1.1 Metabolism

1.1.1 Plant Metabolism

On plants, thiodicarb degrades to methomyl following application, yielding field residues of methomyl.

The 2001, Joint Meeting on Pesticide Residues (JMPR) reports on metabolism studies conducted on cabbage, corn and tobacco in the laboratory and on cabbage and corn in the field, show that the degradation pathway of methomyl is similar in the various crops studied. The JMPR concluded that methomyl is rapidly metabolized in plants and incorporated into natural products.

A summary of their review follows.

The metabolism of ^{14}C methomyl was studied in corn, cabbage and cotton under field conditions.

Cabbage
Field-planted cabbage approximately 6 weeks old received 8 treatments of ^{14}C methomyl at 0.56 kg a.i./ha (1.14-fold Canadian maximum registered rate [CMRR]) with a specific activity of 0.458 µCi/mg. Plants were harvested eight days after the last application. The outer leaves of cabbage heads contained most of the residues, of which 3 to 4% of the TRR was methomyl, while the head contained approximately 2 to 3% of the TRR. Methomyl oxime was not detected in the head or leaves.

Corn
Sweet corn plant approximately eight weeks old received seven weekly treatments of ^{14}C methomyl at 0.56 kg a.i./ha (1-fold CMRR) with a specific activity of 0.222 µCi/mg. Corn ears and fodders were harvested at an early mature stage eight days after the last application. Corn grain contained no methomyl or methomyl oxime.

Cotton
Field-grown cotton leaves were treated with a 50 µg of ^{14}C methomyl in an aqueous solution containing a wetting agent and harvested 0, 4, 8, 24, 48, 96 and 192 hours later. Methomyl was the only component identified on the cotton leaf surface.

Experiments conducted on field show that no methomyl S-oxide, methomyl S,S-dioxide or methomyl oxime (*S*-methyl-*N*-hydroxythioacetimidate [MHTA]) was found in cabbage leaves/heads or in corn fractions.

Tobacco
In order to determine possible translocation to untreated parts of a plant, ^{14}C methomyl was sprayed on tobacco leaves. After three days, no radioactivity was detected in any extracts except the leaves originally treated. After seven days, all segments contained residues indicating a limited foliar translocation of methomyl. Radioactivity level in the untreated segments was less than 1% of the residual radioactivity on the treated leaf.

In the laboratory studies conducted with radioactive ^{14}C methomyl, the ratio of the volatile compounds ^{14}C carbon dioxide to ^{14}C acetonitrile is of 1:1 in cabbage and tobacco, and of 1:4 in corn. Tobacco plant roots exposed to a solution of radiolabelled compound for 28 days absorbed 25% (6% of the TRR) of the available radiolabel over four weeks. The 75% remaining may be lost by volatilization (CO_2 and acetonitrile in equal proportion).

Carbon dioxide and acetonitrile are the major breakdown products of methomyl in plant. They are reincorporated into natural plant constituents in cabbage and corn, such as fatty acids. Due to its volatility, acetonitrile was not found as a terminal residue in plants. CO_2 is the main degradate under aerobic conditions. Methomyl on soil is also subject to photodegradation. Maximum concentration of acetonitrile, the major photolysis degradate, is found after 30 days in soil. No apparent conjugates were observed in any plant metabolism studies. The only terminal residue specifically detected was methomyl. No direct metabolites of methomyl were detected in plants.

Methomyl oxime, if present, occurs as a minor metabolite.

The PMRA requests the registrant to provide acceptable plant metabolism studies or the USEPA Data Evaluation Reports (DERs) to confirm the nature of the residues. Pending receipt of these studies, the PMRA will accept the JMPR review.

1.1.2 Livestock Metabolism

The 2001 JMPR reports on metabolism studies conducted on livestock, including goats, cows and poultry. A summary of their review follows.

Goats and cows
The metabolism of [^{14}C]methomyl has been examined in ruminants in three separate studies (two on goats and one on cows).

In the first study reviewed by JMPR, a lactating goat was given [^{14}C]methomyl by capsule twice a day for 10 days at doses equivalent to 20 ppm (0.6-fold maximum theoretical dietary burden [MTDB]) in the feed. Milk, blood, urine and faeces were sampled daily and tissues within one day of the last dose. No methomyl or methomyl oxime was detected in any of the samples. Approximately 16% and 7% of the radioactivity was excreted in the urine and faeces, respectively and about 8% appeared in the milk and 17% in exhaled air. Residues in the milk reached a plateau after three days equivalent to approximately 2 mg/kg as methomyl, and the lactose contained about 11–13%, hexane extracts, containing the triglyceride components, 26–37% and the casein component 8–9% of the ^{14}C in the milk. This indicates that methomyl had been completely broken down and incorporated into milk constituents. [^{14}C]acetonitrile was identified as a volatile metabolite in milk and blood.

Examination of the liver samples demonstrated that the radioactivity derived from methomyl was found in glycerol, glycerol-3-phosphate, fatty acids, neutral lipids and insoluble protein, indicating a metabolic pathway via acetonitrile and acetate into the naturally occurring constituents in the liver.

In the second study reviewed by the JMPR, a lactating cow was dosed twice daily by capsule for 28 days with [^{14}C]methomyl at a rate equivalent to 8 ppm (0.25-fold MTDB) in the feed. Milk samples were collected each day and selected tissues were taken within 24 hours of the last dose. Radioactivity appeared in the milk within one day and reached a plateau of 0.5 mg/kg equivalents within six days, mostly because of the reincorporation of the radiolabel into fatty acids, lactose and other acetate-derived products. No methomyl or methomyl oxime was detected; acetonitrile accounted for about 25% of the radioactivity. The highest concentrations of radioactivity, equivalent to 9.23 mg/kg, were in the liver, with only 2.01 mg/kg in the kidneys and lower concentrations in fat and muscle. Most of the radioactivity was considered to be the result of reincorporation of the radiolabel as acetate into natural constituents. No methomyl was detected in tissues.

A definitive study of metabolism in goats confirmed the results of earlier studies on metabolism in goats and cows. A lactating goat was dosed orally for three consecutive days with radiolabelled methomyl at a concentration of about 160 ppm (4.8-fold MTDB) determined on the basis of actual feed consumption. About 30% was collected as expired volatile compounds (18% $^{14}CO_2$ and 13% [^{14}C]acetonitrile). The concentrations of radiolabel in milk and tissues were adequate to permit isolation and identification of metabolites (12 mg/kg of liver, 5 mg/kg of kidney, 1.5 mg/kg of muscle, 0.32 mg/kg of fat, 9 mg/kg of milk). Methomyl, methomyl *S*-oxide, methomyl *S*, *S*-dioxide, methomyl oxime and hydroxymethyl methomyl were not detected in any tissue or in milk, with a limit of detection of 0.007–0.018 mg/kg. Radiolabelled acetamide and thiocyanate were found in all tissues and milk, the latter constituting 7–50% of the total radiolabelled residue in the matrices.

Further characterization of the residues in tissues and milk indicated extensive incorporation of the radiolabel into natural components. About 30% of the TRR in milk was shown to be associated with fatty acids, and about 10% was [^{14}C]lactose. About 13% of the TRR in muscle, liver, kidney and fat was shown to be in amino acids.

Poultry

The metabolism of [^{14}C]- or [^{13}C]methomyl was studied in white Leghorn laying hens dosed orally for three consecutive days at a rate equivalent to 45 ppm (23.7-fold MTDB) in the diet. Respired acetonitrile and CO_2 accounted for > 50% of the administered dose. The concentrations of equivalents of radiolabelled material in eggs and tissues were: 3 mg/kg in liver, 0.5 mg/kg in muscle, 0.8 mg/kg in fat, 1.5 mg/kg in egg white and 2 mg/kg in egg yolk. Methomyl and methomyl oxime were not detected in any tissue or in egg (Limit of detection, 0.007–0.015 mg/kg.) Acetamide was found in egg white, and acetonitrile was found in all matrices, constituting 89% of the TRR in egg white.

Further characterization of the radiolabelled residue revealed that 60% of the TRR in egg yolk was associated with lipids, 87% with fat and 32% with liver. Small amounts (3% TRR) in the eggs and tissues were characterized as radiolabelled amino acids.

The USEPA concluded that the qualitative nature of the residue in animals is adequately understood based upon acceptable ruminant and poultry metabolism studies. The USEPA also determined that residues of acetamide and acetonitrile resulting from the application of methomyl to crops are not residues of concern in animals and will not be regulated.

It was concluded that certain metabolic products such as acetonitrile undergo further reactions, with the carbon components being incorporated into natural body constituents such as fatty acids, neutral lipids and glycerol, as shown in ruminants. The metabolic pathway in poultry and ruminant is similar. The main pathway involves conversion of methomyl to the volatile metabolites acetonitrile and carbon dioxide, with further metabolites such as a variety of natural products.

Based on USEPA and JMPR reviews, the PMRA concludes that the metabolism of methomyl is adequately understood in animals, and that similar mechanisms exist in rats, monkeys, ruminants and hens. Methomyl is degraded to acetonitrile, acetamide and CO_2, and these metabolites are incorporated into natural products. Methomyl oxime is a probable intermediate, but neither it nor methomyl showed any propensity to bioaccumulate over the duration of the studies. In poultry and goat metabolism studies, acetonitrile was detected in all samples.

The PMRA requests the registrant to provide acceptable animal metabolism studies and/or the USEPA Data Evaluation Reports to confirm the nature of the residues. Until receipt, the PMRA will accept the USEPA and JMPR animal metabolism reviews.

1.1.3 Residue Definition

The qualitative nature of residues in plants and animals is well understood. Based on the cabbage, corn, cotton and tobacco studies previously reviewed, the residue definition is the parent compound, methomyl. The residue definition in plants is methomyl, per se.

Based on cow, goat and hen metabolism studies, the residue definition was established as the parent compound. The residue definition in animals is methomyl, per se.

Degradation of thiodicarb in plants and in livestock lead to the formation of its metabolite, methomyl.

1.2 Analytical Methods

1.2.1 Methods for Residue Analysis of Plants and Plant Products

The USEPA stated that an adequate analytical methodology is available for data collection and enforcing tolerances of methomyl. Method I in the *Pesticide Analytical Manual*, Volume II, is a gas liquid chromatography/sulfur microcoulometric (GLC/SMC) detection method that has undergone a successful USEPA method validation on corn, leafy vegetables and fruiting vegetables. This method involves solvent extraction, clean-up by liquid-liquid partitioning and a base hydrolysis of methomyl residues to methomyl oxime. Acidified residues of methomyl oxime are then partitioned into an organic solvent and determined by GLC using a sulfur microcoulometric detector. The limit of detection is 0.02 ppm for plant commodities.

A high pressure liquid chromatography (HPLC)/fluorescence detection method (Method AMR 3015-94) has also been proposed as an enforcement method. For this method, methomyl residues are extracted into water: acetone, solvent partitioned and cleaned up using a Florisil

column. Residues of methomyl are then quantified by HPLC using post-column hydrolysis and derivatization with o-phthalaldehyde followed by fluorescence detection. This method has recently undergone a successful USEPA method validation using dry pea seeds, sorghum hay, and sugar beet foliage. The validated limit of quantitation is 0.02 ppm.

Data from analysis of methomyl residues in plants have been collected using Method I or modifications of Method I, which included modifications to the clean-up procedures and/or use of a flame photometric detector with a sulfur filter (FPD-S) instead of the microcoulometric detector. Data have also been collected using variations of the adequate HPLC/fluorescence detection method. These methods and the commodities are described in Table 1 below.

The PMRA requests the registrant to provide methods for residue analysis of plants.

Table 1 Residue Analytical Method

Analytical Method	Commodities	Limit (ppm)
GLC/sulfur microcoulometric or flame photometric detector with sulfur filter	Corn, leafy vegetables and fruiting vegetables	0.02 (detection)
HPLC/fluorescence	Dry pea seed, sorghum hay and sugar beet foliage	0.02 (quantitation)

1.2.2 Methods for Residue Analysis of Food of Animal Origin

The USEPA Reregistration Eligibility Decision document stated that data from the recent ruminant feeding study were collected using a modification of the above HPLC/fluorescence detection method. Methomyl residues were extracted and purified using solid-phase extraction and liquid-liquid partitioning. Residues were then quantified by HPLC/fluorescence detection following post-column derivatization. The reported limit of quantitation was 0.01 ppm in milk and meat commodities.

Methods were described for the determination of methomyl in plant and animal commodities. The original methods for plant commodities consist of extraction with an organic solvent, liquid–liquid partition and hydrolysis with sodium hydroxide. The latter converts methomyl and thiodicarb to methomyl oxime. The final extract is analyzed by GC, usually with a flame photometric detector in the sulfur mode.

The more recent method is based on HPLC. The plant matrix is extracted with solvent, cleaned up on a Florisil column and analyzed by HPLC with post-column reaction to convert separated thiodicarb and methomyl to methylamine. Methylamine is derivatized (on-line) and detected by fluorescence.

The GC method has been validated for numerous plant commodities at a limit of quantitation of 0.02 mg/kg. The HPLC method and its modifications have been validated at an limit of quantitation of 0.02 mg/kg for methomyl.

Similar GC and HPLC methods exist for the determination of methomyl in meat, milk, poultry and eggs. The limits of quantitation for the GC method are 0.080 mg/kg for liver, 0.080 mg/kg for kidney, 0.020 mg/kg for muscle and 0.040 mg/kg for fat. Difficulties were experienced in obtaining acceptable recoveries from milk. The HPLC method has a limit of quantitation of 0.02 mg/kg or 0.01 mg/kg, depending on the extent of sample preparation.

The PMRA requests the registrant to provide methods for residue analysis of food of animal origin.

1.2.3 Multiresidue Analytical Method

The Canadian Food Inspection Agency (CFIA) multiresidue method uses an acetonitrile extraction procedure with a solid phase extraction clean-up and analysis by HPLC-fluorescence detection. The Limit of detection is 0.0018 ppm and the limit of quantitation is 0.006 ppm, based on spike recovery from apples.

The USEPA RED for methomyl indicated that, according to USFDA PESTDATA database (*Pesticide Analytical Manual*, Volume I, Sections 242.2 and 232.4), methomyl is completely recovered using United States Food and Drug Administration Multiresidue Protocols A and D.

Table 2 Multiresidue Analytical Method

Methomyl		% Recovery in Apples			LOD (3-fold SD)	LOQ (10-fold SD)
Diluting Solvent	Spike Level	Mean	n	Standard Deviation (ppm)		
Methanol	0.01	108	7	0.0006	0.0018	0.006

1.3 Food Residues

1.3.1 Storage Stability

Storage Stability Data – Plants

Storage stability data are required to validate the stability or rate of decomposition of the residue definition in or on the raw agricultural commodity or processed commodity between the time of harvest or sample collection and the final analysis of the residue.

Storage stability information in the PMRA files for methomyl residues was limited to residues from snap beans. The study covered a 30 month storage period with samples stored at temperatures at or below -17°C. No other freezer stability studies are on file.

The USEPA stated that available data indicate that methomyl is stable in apples, broccoli, corn, oranges (halves) stored at -20°C for up to 24 months; grapes stored at -20°C for up to 27 months; succulent beans stored at -18°C for up to 30 months; beets and beet foliage stored at -10°C for ~1 year; milk stored at -20°C for up to 22 months; mint hay stored at -10°C up to 6 months; mint oil stored at -20°C up to 5 months; and tobacco leaves stored at -18°C for up to 83 days.

Methomyl declined in fortified chopped oranges stored at -20°C by 30% within 6 months, -60% within 12 months, and by >80% within 24 months.

The PMRA and the USEPA have noted a contradiction about the storage of oranges. The registrant should provide information to explain this contradiction. "Oranges stored at -20°C for 24 months showed a stability of methomyl and also a reduction by more than 80%."

The PMRA requests the registrant to provide acceptable storage stability data and/or the USEPA DERs to confirm the nature and the magnitude of the residues in plants.

Storage Stability Data – Livestock
Data submitted with a ruminant feeding study indicate that methomyl is stable at <-70°C in liver for 5.4 months and in muscle and milk for 6 months. However, methomyl was found to be unstable in beef liver fortified at 0.2 mg/kg and stored at -4°C. Methomyl residues decreased 40–60% when stored at room temperature for up to eight hours and residues decreased to 0% within two weeks.

The PMRA requests the registrant to provide acceptable storage stability data and/or the USEPA data evaluation reports (DERs) to confirm the nature and the magnitude of the residues in livestock.

1.3.2 Crop Residues

No residue decline studies are on file for methomyl. Although combined residue decline and magnitude of residue studies in pome fruits were submitted to support an use expansion of methomyl to pears, the decline studies could not be used for Canadian purposes as the studies were conducted in European countries. The similarities of the environmental conditions (temperature, rainfall, soil characteristics) on European sites compared to Canadian growing regions could not be assessed and applicability could not be determined.

Existing residue data are dated and do not fully satisfy the requirements as described in Regulatory Directive DIR98-02, *Residue Chemistry Guidelines*. The technical registrant is asked to provide confirmation that residue field trial data for all commodities meet contemporary standards by submitting the appropriate data and/or USEPA Data Evaluation Reports.

Methomyl residues resulting from application of both thiodicarb and methomyl were considered in the dietary risk assessment.

1.3.3 Livestock Residues

The JMPR has reviewed two studies conducted on dairy cows in 1995.

In the first study, twelve lactating Holstein dairy cattle were feed twice daily and for 28 days with capsules of methomyl containing the equivalent of 0 ppm, 8.1 ppm (0.24-fold MTDB), 33.7 ppm (1-fold MTDB) or 85.8 pm (2.6-fold) maximum theoretical dietary burden (MTDB). Milk samples collected daily and tissues at the end of the study were stored at -70°C to preclude

degradation of methomyl. Methomyl was not found at the limit of quantitation of 0.01 mg/kg in any tissue or milk samples from cows at any feeding levels.

In the second study, twelve lactating cows were dosed twice daily with a mixture of [^{14}C]methomyl and unlabelled methomyl for 28 days at feeding levels equivalent to 0, 2 ppm (0.06-fold MTDB), 24 ppm (0.7-fold MTDB) or 80 ppm (2.4-fold MTDB) in the diet, based on monitored feed consumption. Milk and tissue samples were stored at -20°C for up to two months before analysis. Methomyl was not found at the limit of quantitation of 0.02 mg/kg in whole milk, cream, skim milk or in any tissue samples.

The PMRA requests the registrant to provide acceptable residue studies and/or USEPA DERs in order to support the registered uses.

1.3.4 Confined Accumulation in Rotational Crops

Data from field accumulation studies on rotational crops will enable the PMRA to determine, under actual field-use conditions, the amount of pesticide residue uptake in rotational crops. Such data are used to establish realistic crop rotation restrictions, i.e. the time from application to a time when rotation crops can be planted, and to provide information for determining whether MRLs are needed in rotational crops.

No rotational crop studies are on file with the PMRA for methomyl and according to the PMRA's *Residue Chemistry Guidelines*, the studies reviewed by the USEPA were considered to be unacceptable.

The PMRA requests the registrant to provide acceptable crop rotation studies in order to support the registered uses.

1.3.5 Processed food

Processing studies are required to determine whether residues in raw commodities may be expected to degrade, reduce or concentrate during food processing. These studies should simulate commercial practices as closely as possible. Processing studies must be conducted if there is likely to be processing of the commodity once it has been imported to Canada or if the processed commodity itself is imported into Canada.

Processing studies for citrus and rapeseed have been reviewed by the PMRA. The citrus processing study examined residues in citrus pulp and pressed liquor but not in the juice while the rapeseed study examined residues when rapeseed was processed into rapeseed meal and oil.

The USEPA concluded that residues of methomyl did not concentrate in any processed commodities except wheat bran (1.9-fold) and apple peel. Studies reviewed by JMPR indicated that methomyl would not concentrate in oils because it is water soluble and the *n*-octanol–water partition coefficient is low.

The processing factors used to refine the dietary risk assessment are presented below in Table 3. In the absence of processing studies, default DEEM™ processing factors were assumed to apply for most commodities in DEEM-FCID™.

The PMRA requests the registrant to provide acceptable processing studies and/or the USEPA Data Evaluation Reports to confirm the values of the processing factors.

Table 3 Processing Factors Used to Refine the Dietary Risk Assessment

Commodity	Processing Factor	Comment
Apple, baked (washed fruit)	0.19	Baking and peeling are consumer procedures
Apple, peeled (washed fruit)	0.83	
Apple juice	0.29	
Apple sauce	0.22	
Citrus (fruit) juice	0.021	Based on orange study
Corn, oil	0.18	
Cotton seed, oil	0.16	Average of thiodicarb factor (0.2) and methomyl factor (<0.12)
Grape wine	0.3	
Orange, juice (citrus)	<0.021	
Peach, baked	0.12	Washing, peeling and baking are consumer procedures
Peanut, oil	0.045	Refined oil
Potato, chips	<0.48	
Potato, peel (dry/wet)	1	
Potato, granules	<0.48	
Soya bean, oil	1	
Tomato juice	0.053	
Wheat flour	0.02	
Wheat bran	1.9	Methomyl is concentrated in wheat bran
Wheat germ	0.92	

Appendix VIII Supplemental Maximum Residue Limit (MRL) Information — International Situation and Trade Implications

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Methomyl MRLs established under the Food and Drug Regulations were not reassessed during this re-evaluation process. A comparison of the Canadian MRLs and the corresponding American tolerances is presented in Table 1. The following conclusions can be made.

- MRLs are only established for the following Canadian registered uses: apple, cabbage, lettuce and strawberry. MRLs have been established to accommodate imports for blueberry, celery, citrus and grape. All other commodities imported and consumed in Canada are covered by the 0.1 general maximum residue limit.

- Generally, the Canadian uses covered by the 0.1 ppm general maximum residue limit have higher corresponding American tolerances.

The Codex Alimentarius Commission has established MRLs for combined residues of methomyl and thiodicarb in/on plant and animal commodities. There is no compliance between Canadian MRLs and Codex MRLs.

Table 1 Comparison between MRLs in Canada and in Other Jurisdictions for Methomyl

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Alfalfa	0.1*	10	10	–	The USEPA stated that separate tolerances, each at 10 ppm, should be established for alfalfa forage and alfalfa hay. No Canadian agricultural use pattern.
		-10			
Apple	0.5	1	2	–	Canadian agricultural use pattern.
		-1	(Pome fruits)		
Asparagus	0.1*	2	2	–	No Canadian agricultural use pattern.
		-2			

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Avocados	0.1*	2	–	–	No Canadian agricultural use pattern.
		-2			
Barley, grain	0.1*	1	0.5	–	Canadian agricultural use pattern.
		-1			
Bean, dry	0.1*	0.1	0.1	–	USEPA stated that storage stability data are required to support the reassessed tolerance. No Canadian agricultural use pattern.
		-0.1			
Bean, succulent	0.1*	2	2	–	Canadian agricultural use pattern.
		-2			
Beet-garden – top	0.1	6	–	–	No Canadian agricultural use pattern.
		-6			
Blueberries	6	6	–	–	No Canadian agricultural use pattern.
		-6			
Brassica	0.1*	6	–	–	USEPA stated that individual tolerances ranging from 2 to 6 ppm have been established for brassica vegetables with registered uses.
Broccoli	0.1*	3	–	7	Canadian agricultural use pattern.
		-3		-7	
Brussel sprouts	0.1*	2	–	–	Canadian agricultural use pattern.
		-2			
Cabbage	5	5	5	7	Canadian agricultural use pattern.
		-5		-7	
Canola	0.1*	–	–	–	Canadian agricultural use pattern.
Cauliflower	0.1*	2	2	7	Canadian agricultural use pattern.
		-2		-7	

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Celery	0.5	3 -3	2	–	No Canadian agricultural use pattern.
Citrus fruit	1	2	1	–	Apply to grapefruit, lemon, orange and tangerine.
Collard	0.1*	6 -6	–	–	No Canadian agricultural use pattern.
Corn	0.1*	0.1 -0.1	0.05	2	Canadian agricultural use pattern.
Corn (sweet)	0.1*	0.1 -0.1	2	2 -2	Canadian agricultural use pattern.
Cottonseed	0.1*	0.1 -0.1	0.5	0.4 -0.2	For thiodicarb, USEPA stated that tolerance can be lowered based upon available data.
Cucurbits	0.1*	0.2 -0.2	0.2 (cucumber)	–	Cucurbit Vegetables Crop Group.
Dandelions	0.1*	6 -6	–	–	No Canadian agricultural use pattern.
Endive (escarole)	0.1*	5 -5	–	35 (Leafy vegetable)	No Canadian agricultural use pattern.
Grapes	4	5 -5	5	–	No Canadian agricultural use pattern.
Grapefruit	1	2	1	–	No Canadian agricultural use pattern.
Kale	0.1*	6 -6	5	–	No Canadian agricultural use pattern.

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Leafy vegetables (exc. beets(tops), broccoli, Brussels sprouts, cabbage, cauliflower, celery, Chinese, cabbage, collards, dandelions, endive (escarole), kale, lettuce, mustard greens, parsley, spinach, Swiss chard, turnip, greens (tops), and watercress)	–	0.2	–	35	The USEPA stated that outdated tolerance for leafy vegetables should be revoked because separate tolerances have been established for leafy vegetables commodities with registered uses.
		(Revoke)			
Leeks	0.1*	3	–	–	The USEPA stated that leeks are covered by the tolerance on green onions.
		(Revoke)			No Canadian agricultural use pattern.
Lemon	1	2	1	–	No Canadian agricultural use pattern.
Lentils	0.1	0.1	–	–	No Canadian agricultural use pattern.
		(0.2)[3]			
Lettuce	2	5	5	35	Canadian agricultural use pattern.
		-5		(Leafy vegetable)	
Melon	0.1*				
Milk	0.1*	–	0.02	–	At or above the limit of determination.

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Mint, hay	0.1*	2	–	–	USEPA stated that separate tolerances, each at 2 ppm, should be established for peppermint tops and spearmint tops.
		-2			
Mustard, greens	0.1*	6	–	–	No Canadian agricultural use pattern.
		-6			
Nectarines	0.1*	5	5	–	USEPA stated that residues in/on nectarines are covered by the tolerance on peaches, according with 40CFR §180.1(h).
		(Revoke)			No Canadian agricultural use pattern.
Oat, grain	0.1*	1	0.5	–	Canadian agricultural use pattern.
		-1			
Onion, green	0.1*	3	0.5	–	No Canadian agricultural use pattern.
		-3	(onion welsh)		
Orange	1	2	1	–	No Canadian agricultural use pattern.
Parsley	0.1*	6	–	–	No Canadian agricultural use pattern.
		-6			
Peaches	0.1*	5	5	–	No Canadian agricultural use pattern.
		-5			
Peanuts	0.1*	0.1	0.1	–	No Canadian agricultural use pattern.
		-0.1			
Peas	0.1*	5	5	–	Peas green, succulent
		-5			Canadian agricultural use pattern.
Pecans	0.1*	0.1	–	–	No Canadian agricultural use pattern.
		-0.1			

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Peppers	0.1*	2			No Canadian agricultural use pattern.
		-2			
Pomegranate	0.1*	0.2	–	–	No Canadian agricultural use pattern.
		-0.2			
Potato	0.1*	–	0.1	–	Canadian agricultural use pattern.
Rye, grain	0.1*	1	–	–	No Canadian agricultural use pattern.
		-1			
Sorghum, grain	0.1*	0.2	0.2	–	No Canadian agricultural use pattern.
		-0.2			
Soybeans	0.1*	0.2	0.2	0.2	Codex: based on thiodicarb use.
		-0.2			
Spinach	0.1*	6	5	–	No Canadan agricultural use patterns.
		-6			
Strawberry	1	2	–	–	Canadian agricultural use pattern.
		-2			
Sugar beet	0.1*	–	0.1	–	No Canadan agricultural use pattern. Tolerance for sugar beet tops is 2 ppm
Swiss chard	0.1*	6	–	–	No Canadan agricultural use pattern.
Tangerine	1	2	1	–	No Canadan agricultural use pattern.
Tomato	0.1*	1	1	–	Codex: baed on thiodicarb use.
		-1			Canadian gricultural use pattern.

Commodity	Methomyl		Methomyl + Thiodicarb	Thiodicarb	Comment
	Canadian MRL (ppm)	American Current tolerance (reassessed) (ppm)	Codex MRL (ppm)	American Current tolerance (reassessed) (ppm)	
Turnips, greens, tops	0.1*	6	–	–	USEPA stated that additional data are required unless the registrant removes turnip green tops from the American labels.
		(TBD)			No Canadian agricultural use pattern.
Watermelon	0.1*	–	0.2	–	No Canadian agricultural use pattern.
Wheat, grain	0.1*	1	0.5	–	Canadian agricultural use pattern.
		-1			

* General Maximum Residue Limit of 0.1 ppm under the Food and Drug Regulation B15.002.

[a] The USEPA reassessed tolerance is tentative pending submission of supporting storage stability data, see Re-registration decision document for methomyl.

Table 2 Residue Definition in Canada and Other Jurisdictions

Jurisdiction	Residue definition	
	Plant	Animal
Canada	Methomyl	Methomyl
United States	Methomyl	Methomyl

Appendix IX Environmental Fate and Toxicology

Table 1 Fate and Behaviour in the Environment

Terrestrial			
Property (study length)	**Test Substance**	**Value**	**Comments**
Abiotic transformation			
Hydrolysis (30 d)	Methomyl	pH 7 – stable pH 5 – stable pH 9 – 30 d or pH 4.5: 392 d pH 6: 378 d pH 7: 266 d pH 8: 140 d	Not an important route of transformation
Phototransformation–Water	Methomyl	1 d	Important route of transformation
Phototransformation on soil	Methomyl	34 d	Not an important route of transformation
Biotransformation			
Biotransformation in aerobic soil (up to 365 d)	Methomyl	silt loam DT_{50} = 30–45 d loam soil DT_{50} = 10.5 d	Slightly persistent Non-persistent
Biotransformation in anerobic soil	Methomyl	static conditions DT_{50} = 14 d dynamic conditions DT_{50} = 2.1 d	
Mobility			
Adsorption or desorption in soil	Methomyl	Kd adsorption: 0.23–1.4 K_{oc}: 5–91	High to very high mobility
Volatility	Methomyl	Vapour pressure: 5×10^{-5} mmHg Henry's law: 1.8×10^{-7} atm m^3/mole	Not likely to volatilize from moist surfaces or water
Soil thin layer chromatography	Methomyl	Rf: 0.52–0.82	Moderately mobile to mobile
Field studies			
Field dissipation	Methomyl	DT_{50}: N/A DT_{90}: N/A	No relevant field studies available

Property (study length)	Test Substance	Value	Comments
Aquatic			
Abiotic transformation			
Hydrolysis	Methomyl	pH 7 – stable pH 5 – stable pH 9 – 3 d or pH 4.5: 392 d pH 6: 378 d pH 7: 266 d pH 8: 140 d	Not an important route of transformation
Phototransformation in water	Methomyl	1d	Important route of transformation
Biotransformation			
Biotransformation in aerobic water systems	Methomyl	DT_{50} = 4 – 5 d	Non-persistent
Biotransformation in anaerobic water systems	Methomyl		

Table2 Toxicity to Non-Target Species

Organism	Exposure	Test Substance	End Point Value	Degree of Toxicity
Invertebrates				
Earthworm	Acute	Lannate 20L	LC_{50}: 7d–165 mg a.i./kg 14d–102 mg a.i./kg	No classification
Earthworm	Acute	Lannate 25WP	LC_{50}: 7d–147 mg a.i./kg 14d–87 mg a.i./kg	No classification
Bee	Contact	Methomyl	LC_{50}: 0.1 µg a.i./bee	Highly toxic
Birds				
Bobwhite quail	Acute	Methomyl	LD_{50}: 24.2 mg a.i./kg bw NOEL: 10 mg a.i./kg bw	Highly toxic
	Dietary	Methomyl	LC_{50}: 1100 mg a.i./kg diet	Slightly toxic
	Reproduction	Methomyl	NOEC: 150 mg a.i./kg diet	Eggs laid; offspring survival
Mallat duck	Acute	Methomyl	LD_{50}: 15.9 mg a.i./kg bw	Highly toxic
	Dietary	Methomyl	LC_{50}: 2883 mg a.i./kg diet	Slightly toxic
	Reproduction	Methomyl	NOEC: 150 mg a.i./kg diet (hatchability)	–

Organism	Exposure	Test Substance	End Point Value	Degree of Toxicity
Mammals				
Rat	Acute oral	Methomyl	LD_{50}: 17–24 mg/kg bw	Highly toxic
	Reproduction (two–generation)	Methomyl	NOEC: 75–100 mg a.i./kg diet (decreased body wt.)	–
Mule deer	Acute oral	Methomyl	LD_{50}: 11–22 mg a.i./kg bw	Highly toxic
Rabbit	Acute oral	Methomyl	LD_{50}: 30 mg a.i./kg bw	Highly toxic
Dog	Acute oral	Methomyl	LD_{50}: 20 mg a.i./kg bw	Highly toxic
Guinea Pig	Acute oral	Methomyl	LD_{50}: 15 mg a.i./kg bw	Highly toxic
Vascular plants				
No data are available, no effects are expected and no data are required for vascular plants				

Table 3 Toxicity to Non-target Aquatic Species

Organism	Exposure	Test Substance	End Point Value	Degree of Toxicity
Freshwater species				
Daphnia magna	Acute 48 hrs	Methomyl	EC_{50}: 28.7 µg a.i./L	Very highly toxic
	Chronic	Methomyl	21 d NOEC: 0.4 µg a.i./L (# of offspring) 28 d NOEC: 1.6 µg a.i./L	No classification
Scuds (*Gammarus pseudolimnaeus*)	Static 96 hrs	Methomyl	LC_{50}: 920 µg a.i./L	Highly toxic
Stonefly (*Isogenus* sp)	Static 96 hrs	Methomyl	LC_{50}: 343 µg a.i./L	Highly toxic
Stonefly (*Skwala* sp)	Static 96 hrs	Methomyl	LC_{50}: 34 µg a.i./L	Very highly toxic
Stonefly (*Pteronarcella badia*)	Static 96 hrs	Methomyl	LC_{50}: 69 µg a.i./L	Very highly toxic
Midge (*Chironomus plumosus*)	Static 48 hrs	Methomyl	LC_{50}: 88 µg a.i./L	Very highly toxic
Rainbow trout	96 hrs acute	Methomyl	LC_{50}: 1600 µg a.i./L NOEC: 600 µg a.i./L	Moderately toxic
Rainbow trout	96 hrs acute	Methomyl	LC_{50}: 2400–3400 µg a.i./L	Moderately toxic
Bluegill sunfish	96 hrs acute	Methomyl	LC_{50}: 1050 µg a.i./L	Moderately toxic
Brook Trout	96 hrs acute	Methomyl	LC_{50}: 1500 µg a.i./L	Moderately toxic
Cutthroat trout	96 hrs acute	Methomyl	LC_{50}: 6800 µg a.i./L	Moderately toxic

Organism	Exposure	Test Substance	End Point Value	Degree of Toxicity
Channel catfish	96 hrs acute	Methomyl	LC_{50}: 530 µg a.i./L	Highly toxic
Largemouth bass	96 hrs acute	Methomyl	LC_{50}: 1250 µg a.i./L	Moderately toxic
Atlantic salmon	96 hrs acute	Methomyl	LC_{50}: 560 µg a.i./L	***Highly toxic***
Fathead minnow	96 hrs acute	Methomyl	LC_{50}: 2800 µg a.i./L	Moderately toxic
Fathead minnow	Early life stage (28 d)	Methomyl	NOEC: 57 µg a.i./L	–
Fathead minnow	Life cycle (193 d)	Methomyl	NOEC: 76 µg a.i./L	–
Carp	48 hrs acute	Methomyl	LC_{50}: 2800 µg a.i./L	Moderately toxic
Marine species				
Mysid (*Mysidopsis bahia*)	Static (96 hrs)	Methomyl	LC_{50} = 230 µg a.i./L	Highly toxic
Eastern oyster – shell deposition (*Crassostrea virginica*)	–	Methomyl	EC_{50} > 140 000 µg a.i./L	Practically non-toxic
Grass shrimp (*Palaemonetes vulgaris*)	–	Methomyl	LC_{50} = 490 µg a.i./L	Very highly toxic
Pink shrimp (*Penaeus duorarum*)	Static (96 hrs)	Methomyl	LC_{50} = 19 µg a.i./L	Very highly toxic
Mud crab (*Neopanope texana*)	Static (96 hrs)	Methomyl	LC_{50} = 410 µg a.i./L	Highly toxic
Sheepshead minnow	96 hrs	Methomyl	LC_{50}: 1160 µg a.i./L NOEC: 530 µg a.i./L	Moderately toxic

Table 4 Screening Level Risk Assessment on Non-Target Terrestrial Species

Organism	Study Type	Test Substance	Endpoint Value	EEC	RQ[1]	Exceeds LOC?
Invertebrates						
Bee	Contact – 48 hrs	Methomyl	LD_{50}: 0.1µg a.i./bee, 0.112 kg a.i./ha)	1.94 kg a.i./ha	17.3	Yes
Birds						
Bobwhite quail	Acute oral	Methomyl	1/10 LD_{50}: 2.4 mg a.i./kg bw	30.3 mg a.i./kg bw	13	Yes
	Dietary	Methomyl	1/10 LC_{50}: 110 mg a.i./kg diet	480 mg a.i./kg diet	3	Yes
	Reproduction	Methomyl	NOEC: 150 mg a.i./kg diet	480 mg a.i./kg diet	4.4	Yes
Mallard duck	Acute oral	Methomyl	1/10 LD_{50}: 1.6 mg a.i./kg bw	2.7 mg a.i./kg bw	1.7	Yes
	Dietary	Methomyl	NOEC: 288 mg a.i./kg diet	93 mg a.i./kg diet	0.2	No
	Reproduction	Methomyl	NOEC: 150 mg a.i./kg diet	93 mg a.i./kg diet	0.3	No
Red-wing blackbird (40 g)	Acute oral	Methomyl	1/10 LD_{50}: 1.0 mg a.i./kg bw	37 mg a.i./kg bw	37	Yes
House Sparrow (13.9 g)	Acute oral	Methomyl	1/10 LD_{50}: 1.3 mg a.i./kg bw	62 mg a.i./kg bw	48	Yes
Rock dove (340 g)	Acute oral	Methomyl	1/10 LD_{50}: 16.8 mg a.i./kg bw	10.7 mg a.i./kg bw	0.6	No
Mammals[2]						
Rat	Acute oral	Methomyl	1/10 LD_{50}: 1. mg a.i./kg bw	167 mg a.i./kg bw	99	Yes
	Dietary	Methomyl	1/10 LC_{50}: 9.9 mg a.i./kg diet (calculated)[3]	978 mg a.i./kg diet	99	Yes
	Reproduction	Methomyl	NOEC: 75 mg a.i./kg diet	1384 mg a.i./kg diet	18	Yes

1 Risk quotient = exposure / toxicity, trigger for a refined assessment is >1 for all organisms.
2 Calculated using daily food intake rate of 0.06 kg/day and body weight of 0.35 kg from study data.
3 LC_{50} = (LD_{50} × 100)/% body weight consumed
LOC: level of concern

Table 5 Screening Level Risk Assessment on Non-Target Aquatic Species

Organism	Exposure	Test Substance	End Point Value (correction factor)	EEC	RQ[1]	Level of Concern Exceeded?
Freshwater species						
Daphnia magna	96 hrs acute	Methomyl	LC_{50}: 28.7 mg a.i./L (½ LC_{50}: 14.3 mg a.i./L)	425.5	30	Yes
	21 days chronic	Methomyl	NOEC: 0.4 mg a.i./L	425.5	1064	Yes
Scuds (*Gammarus pseudolimnaeus*)	Static 96 hrs	Methomyl	LC_{50}: 920 µg a.i./L (½ LC_{50}: 460 µg a.i./L)	425.5	0.92	No
Stonefly (*Isogenus* sp)	Static 96 hrs	Methomyl	LC_{50}: 343 µg a.i./L (½ LC_{50}:171.5 µg a.i./L)	425.5	2.5	Yes
Stonefly (*Skwala* sp)	Static 96 hrs	Methomyl	LC_{50}: 34 µg a.i./L (½ LC_{50}: 17 µg a.i./L)	425.5	25	Yes
Stonefly (*Pteronarcella badia*)	Static 96 hrs	Methomyl	LC_{50}: 69 µg a.i./L (½ LC_{50}: 34.5µg a.i./L)	425.5	12	Yes
Midge (*Chironomus plumosus*)	Static 48 hrs	Methomyl	LC_{50}: 88 µg a.i./L (½ LC_{50}: 44 µg a.i./L)	425.5	9.7	Yes
Bluegill sunfish	96 hrs acute	Methomyl	LC_{50}:1050 µg a.i./L (1/10 LC_{50}: 105 µg a.i./L)	425.5	4	Yes
Rainbow trout	96 hrs acute	Methomyl	LC_{50}: 1600 µg a.i./L (1/10 LC_{50}: 160 µg a.i./L)	425.5	2.7	Yes
Brook Trout	96 hrs acute	Methomyl	LC_{50}: 1500 µg a.i./L (1/10 LC_{50}: 150 µg a.i./L)	425.5	2.8	Yes
Cutthroat trout	96 hrs acute	Methomyl	LC_{50}: 6800 µg a.i./L (1/10 LC_{50}:680 µg a.i./L)	425.5	0.6	No
Channel catfish	96 hrs acute	Methomyl	LC_{50}: 530 µg a.i./L (1/10 LC_{50}: 53 µg a.i./L)	425.5	8	Yes
Largemouth bass	96 hrs acute	Methomyl	LC_{50}: 1250 µg a.i./L (1/10 LC_{50}: 125 µg a.i./L)	425.5	3.4	Yes
Atlantic salmon	96 hrs acute	Methomyl	LC_{50}: 560 µg a.i./L (1/10 LC_{50}: 56 µg a.i./L)	425.5	7.6	Yes
Fathead minnow	96 hrs acute	Methomyl	LC_{50}: 2800 µg a.i./L (1/10 LC_{50}: 280 µg a.i./L)	425.5	1.5	Yes
Fathead minnow	Early life stage (28 days)	Methomyl	NOEC: 57 µg a.i./L	425.5	7.5	Yes
Fathead minnow	Life cycle (193 days)	Methomyl	NOEC: 76 µg a.i./L	425.5	5.6	Yes

Organism	Exposure	Test Substance	End Point Value (correction factor)	EEC	RQ[1]	Level of Concern Exceeded?
Carp	48 hrs acute	Methomyl	LC_{50}: 2800 µg a.i./L (1/10 LC_{50}: 280 µg a.i./L)	425.5	1.5	Yes
Amphibians[2]						
Amphibians	96 hrs acute	Methomyl	LC_{50} for channel catfish (most sensitive species): 530 (1/10 the LC_{50}: 53 µg a.i./L)	2263	42	Yes
	21 d	Methomyl	NOEC for ELS study with fathead minnow: 57 µg a.i./L	2263	40	Yes
Marine species						
Eastern oyster – shell deposition (*Crassostrea virginica*)	–	Methomyl	EC_{50} > 140 000 µg a.i./L	425.5	<<1	No
Crustacean (mysid)	96 hrs	Methomyl	LC_{50}: 230 µg a.i./L (½ LC_{50}: 115 µg a.i./L)	425.5	3.7	Yes
Grass shrimp (*Palaemonetes vulgaris*)	–	Methomyl	LC_{50} = 490 µg a.i./L (½ LC_{50}: 245 µg a.i./L)	425.5	1.7	Yes
Pink shrimp (*Penaeus duorarum*)	Static 96 hrs	Methomyl	LC_{50} = 19 µg a.i./L (½ LC_{50}: 9.5 µg a.i./L)	425.5	44.8	Yes
Mud crab (*Neopanope texana*)	Static 96 hrs	Methomyl	LC_{50} = 410 µg a.i./L (½ LC_{50}: 205 µg a.i./L)	425.5	2	Yes
Sheepshead minnow	96 hrs	Methomyl	LC_{50}: 1160 µg a.i./L (½ LC_{50}: 116 µg a.i./L)	425.5	3.7	Yes

1 Acute RQ = EEC in a 80-cm deep water body / (EC_{50}/ LC_{50} invertebrates ÷ 2 or LC_{50} ÷10 for fish); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC.

2 15 cm depth used for EEC calculation and fish toxicity endpoint used as surrogate.

Table 6 Risk Assessment on Non-Target Species Considering Drift from Spray Area

Organism (exposure)	Test Substance	Endpoint (mg a.i./L)	EEC based on % drift for ground boom and aerial sprayer application[1]	RQ	LOC Exceeded?	Factors	Mitigation Required?
Terrestrial							
Birds (Bobwhite quail)	Methomyl	Acute oral: 1/10 LD_{50}: 2.4 mg a.i./kg bw	Ground: 1.8 mg a.i./kg bw	0.8	No	Birds are at acute and dietary risk from exposure to off-field spraydrift from aerial application of methomyl, as well as at chronic reproductive risk. Ground application drift does not pose a risk to some larger birds, such as the bobwhite quail.	
			Aerial: 18 mg a.i./kg bw	7.5	Yes		
		Acute dietary: 1/10 LC_{50}: 110 mg a.i./kg diet (calculated)	Ground: 28.8 mg a.i./kg diet	0.3	No		
			Aerial: 288 mg a.i./kg diet	2.6	Yes		
		Reproduction: NOEC: 150 mg a.i./kg diet	Ground: 28.8 mg a.i./kg diet	0.2	No		
			Aerial: 288 mg a.i./kg diet	1.9	Yes		
Birds (house sparrow)	Methomyl	Acute oral: 1/10 LD_{50}: 1.3 mg a.i./kg bw	Ground: 3.7 mg a.i./kg bw	2.8	Yes	Small birds are at acute risk from exposure to off-field spraydrift from ground and aerial application.	
			Aerial: 37 mg a.i./kg bw	28	Yes		

Organism (exposure)	Test Substance	Endpoint (mg a.i./L)	EEC based on % drift for ground boom and aerial sprayer application[1]	RQ	LOC Exceeded?	Factors	Mitigation Required?
Mammals (Rat)	Methomyl	Acute oral: 1/10 LD_{50}: 1.7 mg a.i./kg bw	Ground: 10 mg a.i./kg bw	5.9	Yes	Small mammals are at acute and chronic risk from exposure to off-field spray drift from ground and aerial applications of methomyl.	
			Aerial: 100 mg a.i./kg bw	59	Yes		
		Acute dietary: 1/10 LC_{50}: 9.9 mg a.i./kg diet (calculated)	Ground: 58.7 mg a.i./kg diet	5.9	Yes		
			Aerial: 587 mg a.i./kg diet	59	Yes		
		Reproduction: NOEC: 75 mg a.i./kg diet	Ground: 83 mg a.i./kg diet	1.1	Yes		
			Aerial: 830 mg a.i./kg diet	11	Yes		

Organism (exposure)	Test Substance	Endpoint (mg a.i./L)	EEC based on % drift for ground boom and aerial sprayer application[1]	RQ	LOC Exceeded?	Factors	Mitigation Required?
Aquatic							
Freshwater invertebrates	Methomyl	Acute: EC_{50}: 28.7 (½ EC_{50}: 14.3)	Ground: 25	1.7	Yes	Freshwater invertebrates are expected to be exposed to off-field concentrations that exceed the threshold for acute and chronic toxicity from both aerial and ground application of methomyl.	Yes
			Aerial: 255	18	Yes		
		Chronic: NOEC: 0.4	Ground: 25	63	Yes		
			Aerial: 255	638	Yes		
Freshwater fish	Methomyl	LC_{50}: 530 (1/10 LC_{50}: 53)	Ground: 25	0.5	No	Freshwater fish can be expected to be exposed off - field to acutely toxic concentrations of methomyl from aerial application.	Yes
			Aerial: 255	4.8	Yes		
Marine invertebrates	Methomyl	EC_{50}: 19 (½ EC_{50}: 9.5)	Ground: 25	2.7	Yes	Marine invertebrates are expected to be exposed to off-field concentrations that exceed the threshold for acute and chronic toxicity from both aerial and ground application of methomyl.	Yes
			Aerial: 255	27	Yes		

Organism (exposure)	Test Substance	Endpoint (mg a.i./L)	EEC based on % drift for ground boom and aerial sprayer application[1]	RQ	LOC Exceeded?	Factors	Mitigation Required?
Amphibians	Methomyl	LC_{50}: 530 (1/10 LC_{50}: 53)	Ground: 136	2.6	Yes	Amphibians are at risk as they are expected to be exposed to off-field concentrations that exceed the threshold for acute and chronic toxicity from both aerial and ground application of methomyl.	Yes
			Aerial: 1360	26	Yes		

[1] Spray drift used for ground application (6%) obtained from data set; spray drift used for aerial application (60%).

Table 7 Risk to Aquatic Organisms from Surface Runoff

Organism (exposure)	Test Substance	Endpoint	EEC[1] (µg a.i./L)	RQ	Level of Concern Exceeded?
Freshwater invertebrates	Methomyl	Acute :½ EC_{50}: 14.3 µg a.i./L	82.1	5.7	Yes
		Chronic: NOEC: 0.4 µg a.i./L	57.8	145	Yes
Freshwater fish	Methomyl	1/10 LC_{50}: 53 µg a.i./L	82.1	1.5	Yes
		Early life stage: 57 µg a.i./L	57.8	1	Yes
Marine invertebrates	Methomyl	½ EC_{50}: 9.5 µg a.i./L	82.1	8.6	Yes
Amphibians	Methomyl	1/10 LC_{50}: 53 µg a.i./L	438	8.3	Yes

[1] EEC 90th percentile concentration (time-frame and scenario) – acute EEC (96 hrs); chronic daphnid and mysid EEC (21 days).

Appendix X Potential Sources in Drinking Water

Concentrations of methomyl in Canadian drinking water sources were modelled using PRZM/EXAMS for surface water and LEACHM for groundwater. Level 2 drinking water values were estimated using crop specific input parameters and reassessing the fate input parameters to choose less conservative vales than in a Level 1 assessment. The acute Level 2 drinking water EECs determined were 65.4 µg/L, 11.3 µg/L, and 1.29 µg/L for drinking water sources supplied by groundwater, from reservoirs and dugouts, respectively. The chronic Level 2 drinking water EECs were 63.4 µg/L, 0.79 µg/L, and 0.08 µg/L for drinking water sources supplied by groundwater, from reservoirs and dugouts, respectively.

The provincial and territorial governments along with Environment Canada and the Department of Fisheries and Oceans were contacted to request water monitoring data for methomyl. Only one data set that was received included detections of methomyl. This data set was from monitoring conducted in the 1980s; thus, was not considered current for this assessment. Methomyl has been detected in surface water and groundwater in the United States; therefore, there is evidence that methomyl can contaminate water resources.